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AN EXPERIMENTAL STUDY OF THE PROPHYLAXIS OF SYPHILIS WITH ARSPHENAMIN, NEO-ARSPHENAMIN AND SULPHARSPHENAMIN *

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A number of clinical reports have appeared in the literature urging the immediate administration (single dose) of arsphenamin or neo-arsphenamin to persons exposed within twenty-four hours or less to syphilitic infection. Regarding the value of this practice, syphilologists are not in general accord. Michel and Goodman [1] were the first American authors to advocate the use of the arsphenamin in this manner. In the foreign literature, two human experimental inoculations and their abortion (one with arsphenamin and the other with the sodium salt of the acetyl derivative of oxyaminophenyl arsinic acid) are recorded. Dr. Magian,[2] in order to establish the value of arsenical injections in the prevention of systematization of *Spirochaeta pallida,* inoculated himself on the forearm with serum obtained from a primary lesion and containing, on dark-field examination, a large number of spirochetes. One hour later, he took an intravenous injection of 0.6 gm. arsphenamin. On subsequent observation, over a period of eleven months, no lesion appeared at the site of injection, and the complement-fixation test remained persistently negative. The second human experiment was that of a young man [3] who sixteen hours after inoculation took, orally, 2 gm. of the sodium salt of the arsenical compound noted above. During a forty-seven day period of observation, no evidences of syphilis developed.

At the fifth Congress of the Northern Dermatological Society held in Stockholm in 1922, Heden [4] reported cases of persons who had had

* From the Research Institute of Cutaneous Medicine.

1. Michel, Leo L., and Goodman, H.: Prophylaxis of Syphilis with Arsphenamin, J. A. M. A. **75**:1768 (Dec. 25) 1920.

2. Darier, J.: Bul. de l'Acad. de méd., May 20, 1919.

3. Levaditi and Navarro-Martin: Compt. rend. Acád. d. Sc., March 27, 1922.

4. Abst. Arch. Dermat. & Syph. **8**:714 (May) 1923.

intercourse with others presenting open lesions of syphilis, and who had taken prophylactic treatment. None of these developed evidences of syphilis. Hecht [5] reports on five cases, those of wives of men recently infected with syphilis, who were given prophylactic neo-arsphenamin treatment (but in a dosage of 1.35 gm. in ten days), none of whom apparently developed syphilis. May [6] reports that prompt prophylactic treatment prevented the systematization of syphilis in two physicians, one whose eye was infected (?) with syphilitic saliva and the other, who cut his finger in puncturing a chancre. There are doubtless many other unreported instances in which the single prophylactic dose was administered and safety thus thought to be assured.

There is considerably more literature concerning the use of several doses, instead of the single dose, of one of the arsenicals, with which this study is not however concerned. Recently, Vecchia,[7] quoted by Mibelli, reported that rabbits inoculated with syphilis will not develop systematization of the disease if given a dose of 0.01 gm. per kilogram of neo-arsphenamin as late as four days after inoculation. With this report our findings are at variance.

As the clinical reports are, in the main, based on presumptive evidence alone, it seemed of value to determine the effects of the arsphenamins in doses equivalent to the adult human dose, under the same time conditions and in rabbits known to be definitely infected with *Spirochaeta pallida*.

EXPERIMENTAL

Table 1 details the results obtained with neo-arsphenamin given in: (*a*) 0.015 gm. per kilogram (equivalent to 0.9 gm. in an adult human being) and 0.045 gm. per kilogram (equivalent to 2.7 gm. in an adult human) single doses three hours after rabbit infection; (*b*) similar single dosage twenty-four hours after infection; (*c*) three doses each 0.015 gm. per kilogram three hours, twenty-four hours and forty-eight hours after infection; (*d*) same dosage twenty-four, forty-eight and seventy-two hours after infection.

The equivalent adult human single dose of neo-arsphenamin, that is, 0.9 m., did not prevent the development of syphilis even when given as early as three hours after the animal had been infected, but three similar doses given as late as twenty-four hours apart did prevent it.

Table 2 details the results obtained with arsphenamin given in: (*a*) 0.01 gm. per kilogram (equivalent to 0.6 gm. in an adult human being) and 0.03 gm. per kilogram (equivalent to 1.8 gm. in an adult)

5. Hecht, H.: Deutsch. med. Wchnschr. **49**:667 (May 25) 1923.
6. May, J.: Rev. méd. de Uruguay **26**:189 (May) 1923.
7. Mibelli: Gior. ital. d. mal. ven. **11**:207, 1922.

TABLE 1.—*Rabbits Treated with Neo-Arsphenamin*

Date Infected	Weight, Gm.	Dose Drug per Kilogram Gm.	Time Between Infection and First Treatment, Hours	Number of Treatments	Interval Between Subsequent Treatments, Hours	Result	Reinfection of Apparently Cured Rabbits: Date of Reinoculation	Reinfection of Apparently Cured Rabbits: Result
10/20/23	2,400	0.015	8	1	..	Syphilis of testicles in 48 days	12/15/23	
10/20/23	2,400	0.045	8	1	..	Negative testicles in 56 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Died 1/4/24, tortion of large colon
10/20/23	2,250	0.015	3	3	24	Negative testicles in 56 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicles in 35 days
10/20/23	2,300	0.015	24	1	..	Syphilis of testicles in 48 days		
10/20/23	2,500	0.045	24	1	..	Negative testicles in 56 days	0.5 c.c. syphilitic testicle emulsion	Syphilis of testicles in 35 days
10/20/23	2,850	0.015	24	3	24	Negative testicles in 56 days	0 5 c.c. syphilitic testicle emulsion	Syphilis of testicles in 35 days
10/20/23	.....	Infected contral		...	..	Syphilis of testicles in 31 days		
10/20/23	.....	Infected contral		...	..	Syphilis of testicles in 23 days		

TABLE 2.—*Rabbits Treated with Arsphenamin*

Date Infected	Weight 11/23/23, Gm.	Dose Drug per Kilogram Gm.	Time Between Infection and First Treatment, Hours	Number of Treatments	Interval Between Subsequent Treatments, Hours	Result	Reinfection of Apparently Cured Rabbits: Date of Reinoculation	Reinfection of Apparently Cured Rabbits: Result
11/23/23	2,360	0.01	3	1	..	Syphilis of testicles in 60 days	1/25/24	
11/23/23	1,965	0.03	2	1	..	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicle in 31 days
11/23/23	1,820	0.01	3	3	24	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicle in 24 days
11/23/23	1,700	0.01	24	1	..	Negative testicles in 45 days; death, 45th day		
11/23/23	3,000	0.03	24	1	..	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis in 24 days
11/23/23	2,060	0.01	24	3	24	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis in 31 days
11/23/23	.....	Infected control		...	..	Syphilis of testicles in 28 days		
11/23/23	.....	Infected control		...	..	Syphilis of testicles in 21 days		

single doses three hours after the rabbits had been infected; (*b*) similar single dosage twenty-four hours after inoculation; (*c*) three doses each of 0.01 gm. per kilogram three hours, twenty-four hours and forty-eight hours after infection; (*d*) the same dosage twenty-four, forty-eight and seventy-two hours after inoculation.

The equivalent adult human dose of arsphenamin, that is, 0.6 gm., did not prevent the development of syphilis even when given as early as three hours after infection, but three similar doses as late as twenty-four hours apart did prevent it.

Table 3 details the results obtained with sulpharsphenamin given in the same dosages and at the same time intervals as neo-arsphenamin.

TABLE 3.—*Rabbits Treated with Sulpharsphenamin*

Date Infected	Weight 11/23/23, Gm.	Dose Drug per Kilogram Gm.	Time Between Infection and First Treatment, Hours	Number of Treatments	Interval Between Subsequent Treatments, Hours	Result	Reinfection of Apparently Cured Rabbits: Date of Reinoculation	Reinfection of Apparently Cured Rabbits: Result
11/23/23	2,270	0.015	3	1	..	Syphilis of testicles in 38 days	1/25/24	
11/23/23	2,300	0.045	3	1	..	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicles in 24 days
11/23/23	2,200	0.015	3	3	24	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicles in 24 days
11/23/23	2,360	0.015	24	1	..	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicles in 35 days
11/23/23	2,260	0.045	24	1	..	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicles in 35 days
11/23/23	2,180	0.015	24	3	24	Negative testicles in 60 days	0.5 c.c. emulsion of syphilitic testicle into each testicle	Syphilis of testicles in 24 days
11/23/23	.....	Infected control		...	..			
11/23/23	.....	Infected control		...	..			

The results obtained with this drug were similar to those obtained with neo-arsphenamin.

All experiments in the negative animals were controlled by reinoculation tests with emulsions of testicular syphilomas containing active spirochetes.

It is, of course, not absolutely possible to reproduce in rabbits the conditions under which man becomes infected with syphilis. But since a great deal of our data concerning human syphilis has been obtained by analogy to syphilis in animals, our findings, on the one hand raise the question of the value of the single prophylactic dose in man and on the other hand, the question of biologic conditions in rabbits requir-

ing much larger doses than the equivalent human doses to secure prophylactic sterilization under the time conditions specified.

Although, as is well known, the therapeutic efficiency of the arsphenamins is not always uniform, it hardly appears possible that all three drugs used in this study should lack in that respect at the same time.

The term "curative dose" in experimental rabbit syphilis refers to that dose which will cause complete resolution and cure (?) of established rabbit scrotal syphilis, as well as sterilization of the contiguous lymph glands. But our studies appear to indicate that the arsphenamins' curative dose is only curative when the rabbit presents definite scrotal lesions. With arsphenamin the "curative dose" is about 0.01 gm. per kilogram; with neo-arsphenamin, it is 0.015 gm. per kilogram, and with sulpharsphenamin it is from 0.15 to 0.05 gm.[8] per kilogram.

The uniform results obtained with the arsphenamins used in this study clearly show that these curative doses will not prevent the development of syphilis when given as early as three hours after infection of the rabbit.

It is known that whatever reactions, immunologic or otherwise, develop in syphilis, develop before the chancre appears. Are these reactions necessary to enhance the therapeutic efficiency of the arsphenamins, at least in rabbits, since the two human experiments already noted were successfully treated?

1714 Pine Street.

8. Voegtlin, Carl: United States Public Health Report, August, 1922.

THE CLINICAL VALUE OF BISMUTH IN THE TREATMENT OF SYPHILIS

THE REPORT OF SOME UNUSUAL REACTIONS FOLLOWING ITS ADMINISTRATION

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Most of the experimental work on the action of bismuth in the treatment of syphilis has been done by Sazerac and Levaditi,[1] although the trypanocidal properties of bismuth were first discovered by Robert and Sauton.[2] Balzer,[3] in 1889, made experiments on dogs, in which he used ammoniacal bismuth citrate. This work was given up because one of the animals developed a severe keratitis, which was attributed at the time to the toxic action of bismuth, although possibly it was due to a concomitant infection, for no such lesions have been produced since bismuth has been used extensively in the treatment of syphilis.

With the internal administration of bismuth, toxic symptoms were practically unknown, but when bismuth treatment of wound was generally practiced, this state of affairs was changed. A number of intoxications have followed, especially under Beck's method of treating tuberculous fistulas. It has been found that these bismuth intoxications were of the nature of metallic poisonings, somewhat resembling those of mercury in their specific protracted course.

Bismuth is eliminated in the urine, feces, bile, saliva and sweat. If the process of elimination is hindered, especially by the kidneys and liver, or if the dose is large or given at short intervals, or if there is a rapid absorption of a small quantity of the drug, we may encounter some of the clinical symptoms of intoxication, viz.: stomatitis (even ulcerative), gingivitis, gastro-enteritis, disturbances of the circulation and temperature, nephritis, loss of weight, irritation and paralysis of the central nervous system. But with the average patient under bismuth treatment, nothing more than the milder forms of mouth symptoms will be encountered, such as the deposits of bismuth on the margin of the gums about the teeth.

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1. Sazerac, R., and Levaditi, C.: Comp. rend. Acad. d. sc. **172**:1391-1392, ——; **173**:338-340, 1921.
2. Robert and Sauton: Ann. de l'Inst. Pasteur. **30**:261, 1916.
3. Balzer, quoted by Levaditi, C.: Presse méd. **30**:633 (July 26) 1922.

The sixty cases reported in this paper, with the exception of two or three, were all chronic. Patients in the primary and secondary stage of syphilis were not included as a routine in this series, as we feel that it has been definitely established that arsphenamin and neo-arsphenamin are superior, and only those patients with secondary syphilis who resisted arsenic are mentioned. The vast majority of these patients showed improvement while under treatment, and with the exception of three cases presenting symptoms of a severe toxemia due to bismuth poisoning, the reactions following its administration were rare.

Potassium bismuth tartrate with butyn, Dermatological Research Laboratories, was used exclusively in the treatment. The average patient received 0.1 gm. once a week, and some with more active lesions, 0.2 gm. The injections were given deep into the gluteal muscles, and great care was taken not to enter the blood stream. There was no local tenderness complained of by the majority of patients, and no infections were encountered. A total of 2 gm. was given with each course, and then a rest period of four weeks was followed by a second course of the same amount. If a third series of twenty injections were given, the rest period was longer. Many of these patients reported irregularly for treatment.

The clinical effect in all patients that tolerated the drug was marked. A few patients with early secondary syphilis that resisted arsenic responded well to bismuth. The effect on tertiary lesions was rapid, in some cases more favorable than with the arsenicals. In neurosyphilis, the relief of meningeal headaches was as prompt as that seen following the administration of arsphenamin. In several cases in which the headaches were not relieved by arsenic, they responded promptly to bismuth. In cerebral syphilis, it has been effective in controlling the convulsions that sometimes accompany paresis and in relieving insomnia and nervousness. In controlling the lightning pains of tabes dorsalis, it has been more effective than arsenic. The majority of the patients that developed arsenical dermatitis responded well to treatment with bismuth.

The result on the Wassermann reaction was fair. Sixteen, or 26.6 per cent. of the patients under treatment gave a negative Wassermann reaction after receiving a total of 4 gm. All but one case showed a reduction by the Kolmer quantitative complement-fixation test after a total ingestion of 2 gm. When one considers the difficulty encountered in reducing a Wassermann reaction in late syphilis, even when the arsenicals are being used, the results obtained in this series of cases were not bad.

SECONDARY SYPHILIS

Three cases have been reported in the literature[4] in which the patients did not respond to the arsenicals. One was a case of ulceration of the palate and other secondary cutaneous lesions. Four injections of bismuth—20 cg. given every third day controlled the lesions, and a total of 2.4 gm. finally resulted in a cure. One patient was thoroughly treated with neo-arsphenamin eight days after the appearance of the chancre, but signs of secondary syphilis appeared, and the Wassermann test was strongly positive. This patient infected his wife, who showed the same resistance to the arsenic treatment. Under treatment with bismuth, their lesions disappeared, and the Wassermann test became negative. A report of a case of secondary syphilis follows, in which the patient was treated by the author.

R. S., a man, aged 24, a chauffeur, reported for examination on June 16, 1923, with marked alopecia over the temporal and occipital regions, mucous patches on the dorsum of the tongue and corners of the mouth. There was a general glandular enlargement and a papulosquamous eruption on the palms of the hands. The Wassermann test was strongly positive.

The primary lesions on the penis had occurred nine and one-half months before. Secondary manifestations followed in eight weeks. He reported for treatment to the Atlantic City clinic at the appearance of the secondary rash. From that time until June 16, 1923, he had received twenty injections of neo-arsphenamin, 0.9 gm. each, with inunctions of mercury, about thirty in all. All during his treatment at the clinic, the lesions of the mouth disappeared and recurred. There was no evidence of hair growth, and the Wassermann test remained strongly positive. The patient received his first injection of 0.15 gm. of bismuth on June 16. When he reported for his second treatment on June 23, there was great improvement. All of the lesons of the mouth had disappeared, and the numbness of the tongue, of which he had previously complained, had disappeared. The hair showed signs of growth. On July 7, 1923, he was given his third treatment. There had been no recurrence of the lesions of the mouth, and the increase of hair was marked. On Aug. 7, 1923, the fourth treatment was given. There was no recurrence of the lesions of the mouth, and a marked growth of hair. The lesions on the hands entirely disappeared after the second injection. The fifth treatment was given on Aug. 14, 1923, there was no recurrence of lesions. The sixth treatment was given on Sept. 1, 1923; there was no recurrence of lesions, and the hair had entirely grown in. Additional treatments with bismuth were given on Sept. 19 and 29, Oct. 22 and Nov. 10, 1923, making a total of ten treatments at long and irregular intervals. The Wassermann reaction was reduced to moderately positive. The patient was seen again by me a few days ago, and there had been no recurrence of clinical lesions.

TERTIARY SYPHILIS

Case 1.—*History.*—P. O., a man, aged 30, colored, a laborer, was brought to the City Hospital on Dec. 15, 1922. His chief complaint was marked dyspnea, almost complete loss of voice and large serpiginous ulceration of the forehead.

4. Gorim, J., and Jégat, Y.: Ann. d. vén., Paris **18**:368 (May) 1923. Gougert, H., and Giray, Gilbert: Paris méd. **13**:209 (March 3) 1923.

The present symptoms were first noticed last December. The first to appear was shortness of breath on exertion. The hoarseness was noticed in May of the same year. At present, he can speak only in a whisper. He had had a primary lesion of syphilis two years before, followed by secondary manifestations. He had received no treatment.

Examination.—He was poorly nourished. The head, with the exception of a large serpiginous ulceration of the forehead, was negative. Examination of the throat showed severe involvement of the vocal cords. There were scattered moist râles at the base of both lungs, due to passive congestion secondary to cardiac decompensation. The left side of the heart was enlarged with a mitral systolic murmur at the apex. The blood Wassermann test was strongly positive.

Treatment and Course.—The patient was put to bed and treatment started on Dec. 22, 1922. One-tenth gram of bismuth was given intramuscularly. On December 26 and 29, two injections were given, and at that time there was marked improvement in the dyspnea. On the latter date, the lesion on the forehead had entirely healed. On Jan. 2 and 10, 1923, he received additional treatment. His lungs by this time had entirely cleared up, and he was breathing normally. His voice sounds had greatly improved. He was allowed to leave the hospital at this time, and instructed to report twice a week to the clinic for treatment. Following this up until June 22, 1923, he had received a total of 3.5 gm. of bismuth, and clinically was in perfect health, going about his daily routine work. There was never any change in the Wassermann reaction, it being strongly positive when he discontinued treatment on June 22.

CASE 2.—*History.*—M. F. A., a woman, aged 72, reported at the Atlantic City Hospital for treatment on Oct. 13, 1923. Her chief complaint was pain and swelling in the left leg with ulcerations. She had first noticed swelling in the left leg three months before; ulcerations followed. There was no history of a primary infection.

The mother had died of tuberculosis at the age of 45; father died of tuberculosis at the age of 55. One sister, aged 75, was living and well. She was married at the age of 27. She had two healthy children, and had had no miscarriages. Her husband died at the age of 45, cause unknown.

Examination.—There was a punched out ulcer on the medial and lower third of the left leg, about 4 inches (10 cm.) in diameter. The destruction was one and one-half inches (3.8 cm.) deep through the fascia and down into the muscular tissue, and there was no tendency to repair. The whole leg was greatly swollen, owing to impairment of the lymph channels. There were two smaller ulcerations over the anterior aspect of the tibia down to the bone. The Wassermann test was strongly positive

Treatment and Course.—Bismuth treatment was started on Nov. 14, 1923, 0.1 gm. of the drug being given every five days. After eight intramuscular injections, the two small ulcers had completely healed. The large one had entirely filled in, and was rapidly epithelizing; it was about 2 inches (5 cm.) in diameter. After the twelfth injection, the lesions had entirely healed.

CASE 3.—*History.*—F. C., a man, aged 49, whose chief complaint was pain beginning at the left hip posteriorly and extending to the foot, had had pain for three years. It generally occurred at monthly intervals and was of several days' duration. He had had a primary lesion of syphilis twenty years before, for which he had received no treatment.

Examination.—There was marked tenderness on pressure over the sciatic nerve. There were no signs of posterior root involvement. The Wassermann reaction was strongly positive.

Treatment and Course.—A diagnosis of syphilitic neuritis was made and treatment with bismuth was started on July 31, 1923, 0.1 gm. being given at weekly intervals. After twelve injections, the pain had entirely disappeared, and the Wassermann test was negative. On Dec. 19, 1923, the second Wassermann test was negative.

NEUROSYPHILIS

CASE 1.—*History.*—F. S., a man, aged 47, a timekeeper, whose chief complaint was convulsive movements followed by a short period of unconsciousness, had had the present symptoms for one month, having one or two attacks each week. There was no history of primary or secondary syphilis. For the past year the patient had been extremely nervous, irritable and depressed. There was loss of memory at times with marked insomnia. The family history was negative. He had been married for the past seven years. His wife had never been pregnant, but was in good health.

Examination.—The patient was a well nourished male. His skin and mucous membrane were normal; there was no glandular enlargement. His right pupil was slightly larger than the left. There was no reaction to light. The mouth was normal, except for a slight tremor of the tongue. The neck, chest and abdomen were negative. The right knee reflex was normal, the left diminished. The Romberg sign was negative. The gait was normal; speech, slow. There was no tremor, and sense of position was good.

The blood Wassermann test and the spinal fluid Wassermann test were strongly positive. The colloidal gold test gave the paretic curve.

Treatment and Course.—The first injection of neo-arsphenamin, 0.3 gm., was given on April 18, 1923. Following this treatment there was no reaction and no improvement. On April 24 of the same year, another injection of 0.45 gm. of neo-arsphenamin was given. Following this injection, there was some twitching of the eye lids and slight frontal headache. The patient felt worse than before treatment was started. On May 2, 1923, a third injection of 0.45 gm. of neo-arsphenamin was given, and on May 4 he had another convulsion followed by unconsciousness, lasting one-half hour.

The first bismuth treatment was given on May 8, 1923, 0.2 gm., and thereafter once a week until 2.2 gm. had been given. The blood Wassermann test following this course of treatment showed no change, but the clinical improvement was marked. The patient lost practically all of his nervousness; his memory and speech became normal, and he was able to return to his usual work. A rest period was given from Aug. 17 to Oct. 1, 1923; during that time the patient enjoyed good health.

The second course of treatment was started on Oct. 1, 0.1 gm. of bismuth being given twice a week until 2 gm. had been given. Following the last course of treatment, the patient continued to enjoy good health, and there has been no recurrence of his old symptoms. On Jan. 15, 1924, the blood Wassermann test showed a moderately positive reaction.

CASE 2.—*History.*—This was a case of cerebral syphilis of the arterial type in which the patient had been under treatment with arsenic and mercury for the past four years. During that time, he had received over 100 injections of arsphenamin and neo-arsphenamin and a considerable amount of mercury by intramuscular injections.

F. G., a man, aged 42, who was in the fruit business, complained chiefly of insomnia, nervousness and loss of weight. The present symptoms had been present at varying intervals since 1920. He had had a primary lesion of syphilis sixteen years before, but he had had no secondary manifestations. He was

under treatment for one and one-half years with mercury internally. On Sept. 17, 1920, he had a stroke involving the entire right side. The family history was negative. He was not married.

Examination.—The patient was a poorly nourished man, with weakness of the right arm and leg. His pupils were equal and reacted to light. The mouth was negative, except for poor teeth. Speech was normal. The chest and abdomen were negative. The knee reflexes on the right were exaggerated. There was no loss of sensation. The right foot dragged slightly. The blood and spinal Wassermann tests were strongly positive.

Treatment and Course.—Bismuth medication was started on June 10, 1923, 0.1 gm. being given weekly. The patient reported irregularly, so that a week or so would elapse at times between treatments. On Jan. 30, 1924, a total of 2.3 gm. had been given. The clinical results have been good. The nervousness and insomnia disappeared after a few treatments had been given, and the patient has gained in health and strength. The blood Wassermann test taken one month following the last treatment showed a moderately positive reaction. This was the first reduction in the Wassermann test in four years.

CASE 3.—*History.*—J. S., a man, aged 35, a fireman, complained chiefly of sharp pains over the body from the ribs down. There was partial loss of locomotion. The pains in the legs were first noticed one and one-half years before he presented himself. He had difficulty when walking in the dark one year before. Girdle pains had been present for the past two months. He denied all history of venereal infection, gonorrheal or syphilitic. He had enjoyed good health until two years ago, when during a fire he was exposed to the cold and wet. The pains were first diagnosed as neuritis, and he was treated for this disease for more than a year before the true condition was ascertained. Neoarsphenamin was administered at long intervals, with no relief from pain. His father died at the age of 68, with "paralysis." His mother was living and well. There were four other brothers, all in good health. He had been married for twelve years; his wife enjoyed good health. The first pregnancy was a miscarriage following a fall. There were four children living and well.

Examination.—The patient was poorly nourished. His pupils were equal, but there was no reaction to light. His mouth was normal, as were the chest and abdomen. Knee reflexes were absent. The Romberg sign was positive. He had marked ataxia with tremor and partial loss of bladder control. The blood Wassermann and spinal Wassermann tests were strongly positive. The colloidal gold test showed the paretic curve.

Treatment and Course.—Treatment was started on Dec. 17, 1923, by giving 0.4 gm. of sulpharsphenamin intravenously. On December 21, there had been no improvement in the lightning pains; in fact, they had been aggravated, so that on that date 0.1 gm. of bismuth was given. Following the injection of bismuth, there was a slight reaction the following morning; the patient had headache and moderate aching along the lower margins of the ribs on both sides. On Dec. 24, 1923, the lightning pains had entirely disappeared, the first time for two days in one year. The improvement in the pains was noted twenty-four hours after the bismuth was given. Four-tenths gram of sulpharsphenamin was given on December 24, and on December 28, the second injection of bismuth, 0.1 gm., was given. On December 31, when the third dose of 0.4 gm. of sulpharsphenamin was given, there had been no recurrence of the lightning pains. On Jan. 4, 1924, the third injection of bismuth was given. After this the bismuth was discontinued until Feb. 9, 1924, on account of a general weakness,

which we thought was the result of too intensive treatment. During that time neo-arsphenamin was substituted for sulpharsphenamin on account of intense itching (no rash appeared). On Jan. 16, 23 and 30, and on Feb. 6, 1924, 0.45 gm. of neo-arsphenamin was given. On January 30, there was a recurrence of the pains in the leg, so bismuth medication was again started on February 9; following this treatment there has been no recurrence of the pains. The idea now is to give 0.1 gm. of bismuth every other week and 0.45 gm. of neo-arsphenamin every week.

This patient to date has gained 20 pounds (9 kg.). He has complete control of his bladder and has lost most of his tremor. His locomotion has greatly improved.

CASE 4.—*History.*—C. K., a woman, aged 22, whose occupation was housework, complained chiefly of severe occipital and frontal headaches and stiff neck. The headaches had occurred at varying intervals for six months. There was no history of primary or secondary syphilis. The family history was negative. She had been married for four years, and had had two miscarriages; she had no living children.

Examination.—She was well nourished. The left pupil was larger than the right. The pupils reacted sluggishly to light. The knee reflexes were slightly exaggerated, the senses dulled. The blood Wassermann reaction was strongly positive. The spinal fluid Wassermann reaction strongly positive. The cell count was high. The colloidal gold test gave the syphilitic curve.

Treatment and Course.—Two-tenths gram of bismuth was given intramuscularly, with complete relief of head symptoms in twenty-four hours. Three days later the same dose was repeated. The patient left the hospital in eight days, feeling well.

CASE 5.—*History.*—J. S., a man, aged 36, a hotel chef, complained chiefly of marked occipital headaches, stiffness of the neck and a feeling of pressure on the top of the head. He first noticed these symptoms in September, 1921. He was relieved entirely for a time with neo-arsphenamin. There was a recurrence of the headaches later, but in a much milder form. The blood Wassermann test after two courses of neo-arsphenamin, fifteen injections each of 0.9 gm., was negative. The spinal Wassermann test was moderately positive. The cell count was light. The colloidal gold test showed the syphilitic curve. He had had a primary lesion on the penis six months before the clinical symptoms of neurosyphilis were noted. The family history was negative. He had been married five years; he had no children. His wife had died recently of some acute infection.

Examination.—This was negative on May 10, 1923.

Treatment and Course.—Bismuth treatment was started on May 11, 1923, at first 0.2 gm., and later 0.1 gm. being given once a week. After the first two injections of bismuth, the headaches had entirely disappeared. A total of 2.3 gm. of the drug were given before the patient left the city. I received a letter from him recently, which stated that he had had no recurrence of his headache and was felling as well as he had ever felt. No further spinal examination has been made.

REACTIONS AND COMPLICATIONS FOLLOWING BISMUTH MEDICATION

None of the patients under treatment developed a stomatitis, possibly because the drug was never given oftener than twice a week. Bluish gray lines on the gums around the roots of the teeth due to the

deposits of bismuth were seen in a few patiets receiving 0.2 gm. a week. Great care was taken to instruct these patients in the proper care of the mouth and teeth, which may have been a factor in reducing symptoms of the mouth. Although bismuth is excreted largely by the kidneys, in few cases were there signs of kidney irritation. It was noted that when albumin was absent before the injections, it did not thereafter appear. A few patients that had albumin before the treatment was started showed improvement, and in some cases the albumin disappeared entirely after a few injections of bismuth. The favorable effect observed in this group was perhaps due to the fact that in these patients there were curable syphilitic lesions in the kidneys. Two patients with a latent nephritis due to a previous scarlet fever tolerated 3 gm. of bismuth without showing further damage to the kidneys. No cases of dermatitis resulting from bismuth were seen by me, as reported by one author.[5]

Three reactions of special interest in this series occurred in one woman and two men. The symptoms were almost similar, and all of the patients were extremely ill for a short period of time.

Case 1.—*History.*—F. C., a woman, aged 24, whose occupation was housework, had latent syphilis. She first came under observation and treatment two years before because she had a postive Wassermann reaction. There was no history of a primary infection. She was married; she had had one miscarriage and had one healthy child.

Treatment and Course.—Treatments with neo-arsphenamin were started when she first reported, 0.45 gm. being given twice a week. After the sixth injection, she developed a severe dermatitis. Treatment was discontinued for six months, and then 0.1 gm. of neo-arsphenamin was given. The skin reaction following this injection was more severe than the previous one, so further treatment with the arsenicals was abandoned. At a later date, mercury was given by intramuscular injections, with marked kidney irritation.

Bismuth treatment was started on Oct. 9, 1923, 0.1 gm. being given every two weeks. No albumin was noted in the urine.

Four hours following the fifth injection of 0.1 gm. of bismuth, the patient developed a marked chill, which was followed by a slight increase in temperature, moderate oppression in the chest and slight pains in the joints, bones and muscles. The following morning, she was feeling better and was up and about, but late the same afternoon the oppression in the chest became marked, with severe pains in the muscles, bones and joints. She had headache and slight nausea, but she did not vomit. The respirations were rapid, and the pulse rate was 104. There was marked distention of the superficial veins of the forehead. These symptoms continued with the same severity until the third day, when they started to subside, but a week had passed before the pains had disappeared entirely from the bones and joints. There was no skin reaction. The urine showed a trace of albumin following this reaction.

Great care was taken in giving all of these injections not to introduce the needle into a vein, so the symptoms would not be explained by the theory of

5. Marcel, Pinard, and Marassi: Bull. et mém. Soc. méd. d. hôp. de Paris **46**:1434 (Nov. 3) 1922.

intravenous administration. This appears to be a case of bismuth poisoning resulting from rapid absorption with faulty elimination, the latter being due to a previous damage of the kidneys and liver, for the patient reacted poorly to all drugs administered.

Case 2.—E. C., a man, aged 33, who had been under treatment since April 10, 1922, was admitted to the hospital with a diagnosis of secondary syphilis. He was given two courses of neo-arsphenamin, the first one consisting of twenty injections, 0.9 gm. each, a second of twelve injections, and twenty-five injections of mercuric salicylate intramuscular. During this treatment no reactions were noted, and clinical improvement was marked.

Bismuth treatment was started on June 15, 1923, 0.1 gm. being given each week. Several hours after the tenth injection, the patient had chills, followed by fever with nausea and vomiting. Oppression in the chest and pains in the joints and bones was marked, and lasted several days. Urinalysis was negative. Following this, mercury was substituted without further reactions.

Case 3.—C. M., a man, aged 41, who was admitted to the hospital with a diagnosis of neurosyphilis, reported first for examination and treatment on March 18, 1922. Until the bismuth treatment was started on July 28, 1923, the patient had received thirty-two injections of neo-arsphenamin, 0.1 and 0.45 gm. each, and seventeen injections of mercuric salicylate intramuscularly, without showing any clinical reaction to either drug.

One-tenth gram of bismuth was given intramuscularly. Four hours after this injection, the patient developed a slight chill of one-half hour's duration. The following morning he had marked oppression in the chest (just as if it were in a vise) with difficult breathing, rapid pulse and with marked aching, mostly in the joints. The elbows and knees were principally affected. There was slight headache and nausea, but the patient did not vomit. Bleeding gums were pronounced, but no ulcers were seen in the mouth. Marked pains were also complained of in the lumbar muscles. The patient was confined to his bed for two days, but the pains and aches did not disappear entirely for two weeks.

On Aug. 25, 1923, the patient was given a second treatment with bismuth, 0.1 gm. The reaction following this second administration of the drug was identical with that following the first, although it was less severe.

Bismuth medication was discontinued after the second reaction. No albumin was found in the urine at any time.

COMMENT

The last two reactions, unlike the first, can hardly be due to faulty elimination, as the arsenicals and mercury were well tolerated. There may have been an accumulation of the drug in the second case and a rapid absorption in the last one to account for the toxic symptoms. They can hardly be ascribed to the Herxheimer reaction, for these two patients had been well treated before bismuth was given, although their blood Wassermann reactions were both moderately positive.

In the treatment with bismuth, it might be advisable to have a roentgenologic examination made before each treatment as a control. In this way, the amount of absorption could be carefully watched.

These reactions should warn us that bismuth is not given without some danger to the patient, and the same care should be exercised in its administration as with arsphenamin and neo-arsphenamin.

CONCLUSIONS

1. Bismuth should not be substituted for arsenic in primary or secondary syphilis, except in patients resistant to arsenical treatment.

2. Bismuth is effective, clinically, in the treatment of all forms of tertiary syphilis.

3. In the treatment of neurosyphilis, bismuth in some cases has proved itself superior to arsenic.

4. Bismuth should be tried in all patients that do not tolerate the arsenicals.

5. Bismuth should be given with caution in all patients with faulty elimination.

6. The absorption of this drug should be carefully studied, and if possible, the number of treatments given should depend on the roentgenologic findings.

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POSTMORTEM FINDINGS IN THE SPINAL CORD IN TWO CASES OF CHRONIC PEMPHIGUS

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It has been suggested at various times that the lesions of chronic pemphigus depended upon a lesion of the central or peripheral nervous system. Literature on the subject [1] is scanty. Darier states that the nervous system is not involved.

The following is a brief record of the findings in the spinal cord in two cases: There were no pathologic changes found in the nerve cells, connective tissue cells, blood vessels, roots or meninges in the sections examined, at the cervical, thoracic and lumbar levels. The methods of Marchi, Weigert and Mallory were used.

CASE 1.—M. F., a Russian Jew, a tailor, whose family history and past history were irrelevant, became ill in March, 1913, nine years before death, which occurred, April 26, 1922. The initial symptoms were itching about the shoulders and the subsequent appearance of blisters over the entire body. These soon showed crusting and scaling, followed by exfoliating. Examination was negative except for the skin condition, which was a scaling and bullous eruption. The mucous membranes were also affected. Prior to death, a secondary infection of the lesions occurred.

CASE 2.—A. B., aged 43, an Austrian Jew, a tailor, whose family history and past history were irrelevant, became ill in March, 1921. He died, May 14, 1922, at which time the body was covered by bullae; many were infected secondarily. There were bullae on the mucous membranes of the tongue, lips and mouth. Itching and pain were present. The Wassermann test was negative. Death occurred from bronchopneumonia.

10 Rue de Castellane, Paris, France.

1. Darier: Précis de dermatologie, Ed. 2, 1923. Besnier, Brocq and Jacquet: La pratique dermatologique, 1902, p. 777 (literature given).

VERRUCA OF THE NAIL FOLD

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The site in which a neoplasm occurs is often the measure of its importance; this is decidedly so of warts when they occur in the nail fold. Previous to the introduction of radiant energy, they were frequently untreatable except by the severe surgical procedure of evulsion of the nail, and clearing out the entire base; and often this radical measure failed, for if they are not entirely eradicated they have the unpleasant attribute of recurrence.

THE ANATOMY OF THE WART

A verruca begins as a minute rounded grayish elevation composed of epithelial cells. As it increases in size, it sinks deeper into the subjacent epithelium, and the blood vessels of the subjacent papillae elongate upward to supply it with nourishment, forming digitate epithelial growths, each with a central core of connective tissue and a blood vessel loop. In some cases, the upward growth of the little tumor is most marked, and in others the downward growth. In a fairly well developed wart of the free surface, if the tip of a curet is pressed against its base, it often may be tipped out of its bed, and it is quite surprising what a deep hole is left. The thicker and denser the epithelium of the locality in which the wart occurs, the greater the depth the wart is capable of extending downward. In the thick epithelium of the sole, warts may attain an extraordinary depth, and this fact must be kept constantly in mind when treating them. For the same reason, they grow down deep on the palmar surfaces of the hands and about the nails, and these also are the only situations—the soles, the palms and about the nails—where warts are painful, and in these localities they may be extremely painful.

THE ANATOMY OF THE NAIL FOLD

The salient feature of the nail fold as far as we are concerned is the overhang of the sharp lateral edge of the nail in the bottom of a groove. This overhang we have seen depicted only twice in the histology of the nail, once by A. Branca [1] and once by Szymonowicz.

1. Branca, A., in Elements d'Anatomie et de Physiologie Medicales, Paris, Landouzy-Leon Bernard, 1921. Salomon, M.: La Peau, Paris, Masson et Cie, 1921, p. 604.

A wart, therefore, in this site is not only situated in the bottom of a trough but also tends to insinuate itself under the overhanging nail edge, constituting a most tantalizing impediment to any mode of treatment.

The dense epithelial covering of a wart is resistant to radiant energy, and this, together with the remoteness of the base of the growth, forms a thick screen necessitating prolonged irradiation with a strong unscreened radium plaque. The danger of causing a radium burn is negligible when the surrounding tissues are carefully shielded by heavy lead accurately fitted around the base of the growth.

UNUSUAL CLINICAL TYPES

There is yet another peculiarity of verrucae in this site, mentioned only, as far as we know, by Gougerot.[2] Usually warts form easily recognizable separate neoplasms of no great dimensions, but around the nail they may spread out into quite a large sheet, forming a sort of flattened corneous tumor quite unlike the ordinary wart. The following case is an excellent example of this clinical variety.

A stenographer, aged 24, consulted us for one of these extensive growths on the terminal side of the right index finger, which became unsightly and interfered with her work. It extended well under the nail and flowed out over the neighboring surface in an irregularly crescentic shape, measuring 17 by 8 mm. The result of treatment was perfect. Nine months afterward a new verruca appeared on the free surface just at the outer edge of the previously affected surface, which was easily managed with the curet and trichloracetic acid. This recurrence shows how persistent the verrucous tendency may be in an area once affected.

Another case of these sheetlike warts occurred in a woman, aged 23. It began in the nail fold of the ulnar side of the right index finger. When we saw it, it had spread out over a somewhat irregular area fully 1 cm. in diameter, with one edge just under the edge of the nail.

As illustrative of another variety, a waitress, aged 29, came to us with warts in the nail folds of a number of fingers, and the individual papillae were so minute that the affection at first was considered to be a hyperkeratosis. Until the diagnosis was rectified, the treatment was of course fruitless.

Some writers suppose that the papillae of a wart are the hypertrophied papillae of the papillary layer of the skin or mucous membrane.

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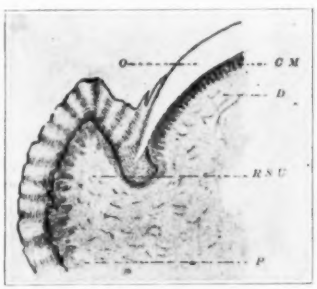
2. Gougerot, H., La dermatologie en clientèle, Paris, A. Maloine et Fils, 1922, p. 750.

If this were exclusively so, no verrucae could occur where no papillae are present. The nail bed has no papillae in the strict sense of the term, but instead has longitudinal grooves in which the nail plate is set, yet undoubtedly verrucae can invade the nail bed, causing riffles in, and more or less extensive separation of, the nail plate.

One of our most interesting cases was that of a man, aged 45, who eight years previously, while working, had abraded the skin on the ulnar side of the dorsum of the terminal joint of the right index finger. It healed, leaving an elevation, which gradually spread to the other side of the finger. When he came to us, there was a solid papillomatous tumor extending around the nail base to the radial side of the finger. It was not painful, and although it bled easily, it was not raw. It



Transverse section of the nail, by A. Branca, showing the overhang of its lateral edge. The heavy dark line is a schematic representation of the stratum lucidum, which joins the nail on its under side. The nail is a very thick stratum lucidum. The illustration gives an excellent idea of how deeply situated the base of a wart in a nail fold lies, and how disadvantageous for the treatment it is when it insinuates itself under the edge of the nail.

O indicates the ungual limb; *CM*, unguous mucous body; *D*, subungual derma; *RSU*, lateral nail fold; *P*, interpapillary epithelial granulation.

was, however, uncomfortable, and he was always picking it. It was rough and desquamative and redder than the normal skin. One hour's exposure to a very strong radium plaque, unscreened, caused it to disappear, and with a restitution so entire that even the normal markings of the skin reappeared.

A rather amusing circumstance occurred in this case. About a week after the treatment was given, the patient telephoned in to tell us that we had better purchase some more radium as that which we had was evidently of no use. We told him to have a little patience. The next day the reaction commenced, and he soon became satisfied that the radium was all right.

We never were convinced that this was a true verruca, and it may have been due to some other kind of infection than that which causes the ordinary variety.

The points to be remembered in the treatment of verrucae are the thickness of the horny layer, requiring a more prolonged irradiation than would ordinarily be considered safe for the skin, and the careful shielding of the surrounding cuticle which is much less thick and much more sensitive.

IS DANDRUFF SEBORRHEAL?*

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We believe that dandruff is not essentially seborrheal; that the combination of seborrhea and dandruff is not so common as to warrant the present classification; that the old pityriasis group should be restored to its original and independent status; that the definition of seborrhea should be standardized, and that the use of the adjective *seborrheal* should be confined to conditions in which seborrhea is essential—not incidental to the morbid picture.

After examining the textbooks on dermatology used in American medical schools, I am inclined to accept the Elizabethan description quoted below as, by comparison, clear and accurate. The word dandriff (dandriffe, dandruff) is of Anglo-Saxon origin, a combination of *tan* meaning tetter and *drof* meaning dirty.[1] Dandruff, then, is "itch-dirt" and is described as follows in what is said to be the first book on midwifery published in the English language.[2]

Of the Causes and Remedies of Dandruffe of the Head.

I will briefly declare the filthinesse of the head called in Latin *Perrigo*, in English the dandruffe of the head, the which is, when at the kembing and scratching of the head, certaine white scales, as it were branne, falleth off from the head, and lyeth very thick among and under the hayre.

The cause of this dandruffe cometh by abundance of flegmaticke humors, commixt with the blood, the which daily and hourly by incessible sweating, evaporeth and issueth out of the pores in the skin that covereth the panbone, and as fast as it issueth forth, dryeth on the outter superfacie of the skin, and there remaineth and gathering together, becometh every day more and more, thereto greatly keeping the forrest of hayre which covereth, harboureth, and retaineth such superfluities, more in those places than in any other, where no hayre groweth (most commonly they that have blacke hayre have more store of dandruffe than others). This humour suffered over long to reigne on the head, destroyeth and corrupteth the rootes of the haires, making them fall off in great plenty, and especially in kembing. And although this superfluity be not cleanely, yet notwithstanding it shall be no wisdome for me to teach, ne any other here-

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* Read before the Section on Dermatology and Syphilology at the Seventy-Fifth Annual Session of the American Medical Association, Chicago, June, 1924.

1. Foster, F. P.: An Illustrated Encyclopaedic Medical Dictionary, New York, D. Appleton & Co., 1891.

2. Raynald, T.: The Birth of Mankinde; Otherwise the Woman's Booke. Set forth in English by Thos. Raynald, Physitian, London. Printed for A. H., and are to be sold by John Morrett, at the two Tuns in little Britaine, 1634.

with encumbered to learne how to stop it, for feare of further inconveniences: but only I counsell you once in ten days, at the least, to wash and scoure the head cleane with good lye wherein let be steeped in a linnen bag, of Annis seed, Commin, dried Rosemary, Fenegreke, and rinds of Pomegranate, of each like much: and beware that after washing of your head yee take no colde before the head be perfectly dryed.

One cannot take two steps in the study of scaly conditions of the scalp without encountering the vexing question of seborrhea. Only three authorities (Jackson and McMurtry, Whitfield and Darier) fail to describe dandruff under seborrhea; and none comes out flat-footed with a statement that seborrhea is not a scaly disease. Yet, realizing that they are stepping on treacherous ground, they all offer a dignified hedge in case someone should ask an embarrassing question. I have come to expect to find a passage under seborrhea sicca something like this:

> While much work has been done tending to prove that the dry form of this condition is neither an eczema nor a seborrhoea and is quite probably due to a specific microorganism, the concensus of opinion is not yet sufficiently crystallized to warrant a change in the classification and it will be continued as in previous editions.

It seems to me that the consensus of opinion has had ample time to jell, and that medical students should no longer be asked to accept a "dry oiliness" and an "oily oiliness" as an adequate classification of the common scalp conditions leading to loss of hair. If a student is inquisitive enough to examine the literature he finds that pityriasis simplex, which is given as a synonym of seborrhea sicca, may quite commonly be found in children of from 6 to 10 years, and begin to wonder whether these unfortunate children are sexually precocious.

His wonder increases when he reverts to his textbook and learns [3] that: "In infants it is at birth more or less general, though variable in quantity, and constitutes the so-called vernix caseosa (also ichthyosis sebacea)." If he turns to another author,[4] he learns that "Aside from ichthyosis congenita neonatorum, or ichthyosis sebacea, with its resultant vernix caseosa, seen in the new-born, crusted or scaly seborrhea is a comparatively rare affection. The sebaceous glands are extremely active throughout early infancy, and neglect of cleanliness is usually promptly followed by the development of seborrheic dermatitis." These are truly astounding statements to find following a more or less emphatic

3. Stelwagon, Henry W.: A Treatise on Diseases of the Skin, Ed. 8, Philadelphia, W. B. Saunders Company, 1918.

4. Sutton, Richard L.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1919.

assertion that seborrhea is a disease of puberty; furthermore, they are entirely incorrect. I quote from one [5] who has gone to the trouble to find out:

> The vernix caseosa is in no sense a glandular fat as Hebra, and more recently Jacquet, have maintained. It presents no free fat. Washed in ether it loses only an inappreciable amount of its weight. Furthermore sebaceous material spread on a slide and stained with osmium is black, while the vernix caseosa treated in the same manner takes instead of black the grayish tint of normal dissociated epidermic cells. Finally, examined under the microscope the vernix shows itself to be formed exclusively of separated epidermic cells without nuclei, which I can best compare to well-stuffed square cushions. I wish to emphasize these facts which show us that which Robin stated in 1860, namely, the vernix caseosa has nothing in common with a fatty exudation and a seborrhoea.

Sharlit [6] has demonstrated that the vernix caseosa has the same hydrogen-ion concentration as normal skin, which would not be the case if it contained more fat.

I mention this matter of the vernix caseosa for several reasons. This material is slippery, but it is not oily; yet men of great accomplishment in dermatology have been content with its feel of oiliness to class it in their books as a form of seborrhea; not only seborrhea, but seborrhea sicca.

By the same rapid method they have arrived at the conclusion that dandruff is oily and therefore seborrheal. And this thesis they maintain as tenaciously as the witness who when asked if he had really meant to testify that the horse was 16 feet high rather than 16 hands high, replied, "If I said sixteen feet, I'll stick to it."

Again, it is a striking illustration of what Darier refers to when he says:

> The meaning of the term seborrhoea has been unreasonably extended by authors, to the point of applying it to all the other manifestations of kerosis, and even, by Hebra, to pityriasis simplex, thereby leading to the enormous confusion which still prevails as illustrated by the commonly used but highly improper terms of seborrhea sicca (for pityriasis simplex), seborrheic eczema (for eczematide) and so forth.

Seborrhea (L. sebum, Gr., ῥοία), a hybrid word, was coined by Fuchs [7] of Göttingen, in 1840. He used this new word to designate what we now call seborrhea oleosa, which he calls seborrhagie, and a cystic seborrhea, under which he describes the comedo.

Before 1840, Biett had applied the term acne sebacée to the condition, and Rayer the term flux sebacé.

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5. Sabouraud, R.: Maladies du cuir chevelu, Paris, Masson et Cie, 1902.
6. Sharlit, Herman: Personal communication.
7. Fuchs, Conrad Heinrich: Die krankhaften Veränderungen der Haut und ihrer Anhange, 1840.

In 1860, Erasmus Wilson redescribed the seborrhea of Fuchs and applied the term steatorrhea; he limited its evolution to the sexual age, and separated from it the seborrheiform maladies of infancy.

All of these writers describe the desquamative processes under other headings, usually pityriasis, with various subdivisions, and considerable confusion with eczema and psoriasis. None of them seems to have associated seborrhea oleosa with loss of hair.

It was not until Hebra [8] published his epoch-making work that seborrhea and the scaling diseases became confused, and because of his great position as founder of the Vienna school of dermatologists, this confusion persists. The quotation follows:

> Seborrhoea consists in a vice of the epidermic secretion (vice of cellular formation) producing sebum which impregnates this membrane and forms either a fatty envelope or accumulates in masses like scales on portions of skin which are in other respects perfectly healthy.
>
> Before passing to the detailed description of the phenomena produced by this cutaneous affection I ought to point out that it may occur in two forms; I designate the first under the name of seborrhoea oleosa seu adiposa and the other under that of seborrhoea sicca seu squamosa.
>
> However different the symptoms of these two varieties may be, there is no difficulty in proving that they are only one and the same disease.
>
> For we observe frequently in one, or in any case, most of the characteristics belonging to each of them.
>
> Furthermore a seborrhoea oleosa may transform itself into a seborrhoea sicca, and finally on submitting the morbid products which appear in these two affections to microscopic and chemical examination, one finds in both cases that they are constituted of exactly the same elements, notably of epidermic cells saturated with fatty globules. The findings are the same whatever may be the seat of the malady, whether it takes the form of a seborrhoea capillitii or of a seborrhoea praeputii or of that called pityriasis furfuracea seu amiantacea or even of a diffuse pityriasis tabescentium, covering a large portion of the cutaneous surface.

Commenting on this quotation Sabouraud [9] says:

> Such is the celebrated text of Hebra. It is easier for us to judge it today than it was in 1870. In any case it is certain that it contains almost as many errors as words. Nothing is rarer than for an oily seborrhoea to change into a dry seborrhoea; it is the contrary that is frequent. Nothing is more different under the microscope from either the histologic or the histochemical standpoint than scrapings from cases of oily and of dry seborrhoea of Hebra. Finally these products differ greatly from those of smegma and still more from those of a pityriasis tabescentium. This clinical melange is, then, one of the strangest and most heterogeneous possible.

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8. Hebra, Ferdinand: A Treatise on Diseases of the Skin, trans. by A. Doyon, 1869.

9. Sabouraud, R.: Maladies du cuir chevelu, Paris, Masson et Cie **2**, 1904.

Yet this idea, followed by Kaposi [10] and modified and elaborated by Unna,[11] was backed by such great names that it has been accepted without question for fifty years, and in textbooks of recent date may be found almost unchanged.

Neither Hebra nor Unna devoted much space to oily seborrhea. Unna denied that it was due to overactivity of the sebaceous glands, and called it "oily hyperhydrosis." Their interest seems to have centered around the idea that seborrhea henceforth must connote a scaling condition. To accomplish this, Hebra confuses a crust with a true scale, and Unna justifies his use of the words seborrhea sicca by claiming that the diminution of the secretory power of the gland causes the excretion of dry scales. A more sweeping repudiation of terms is hard to imagine. Unna goes further; he describes a seborrheic eczema which gradually comes to include a veritable horde of previously distinct conditions, and during its elaboration he makes of eczema a bacillary disease, thereby ignoring the view of the English school, which is now generally accepted, that the primary lesion of eczema is a *sterile* vesicle.

Here, then, we have a striking illustration of the persistence of words with a complete change in their basic meaning. One is reminded of the Holy Roman Empire, which was neither holy, Roman, nor an empire. In order to have a meeting of the minds of reader and writer, it is obviously necessary to define certain words and the conditions they indicate. This is always a bold venture, and may easily antagonize the reader, but nothing can be accomplished without it.

STEATORRHEA

Steatorrhea (Gr., στέαρ + ῥοία) is a sebaceous hypersecretion. It occurs physiologically at puberty, and is most marked where the oil glands are most numerous. If uncomplicated by infection, it does not produce hypertrophy of the sebaceous glands, and gradually decreases with the advent of middle age. It is noninflammatory.

SEBORRHEA

Seborrhea (L., sebum Gr., ῥοία) is wrongly used as a synonym for steatorrhea, and correctly, to designate a disease which, in combination with various infections and functional derangements, may present widely different clinical appearances. In its simple form, seborrhea is characterized by a sebaceous hypersecretion, enlargement of the pilosebaceous orifices and, on hairy surfaces, a progressive alopecia. Clinically, the presence of the disease can be demonstrated by squeezing between the

10. Kaposi, Moritz: Pothologie et traitement des maladies de la peau, trans. by Besnier and Doyon, 1886.

11. Unna, P. G.: Seborrhoeal Eczema, J. Cutan. Dis. **5**:449, 1887.

finger-nails a fold of skin in a seborrheic area. It will be observed that the sebaceous pore yields, under this pressure, a vermicelli-like filament, and this filament can be readily spread on a coverglass, washed with ether and stained with almost any basic dye. There will then be found on microscopic examination innumerable microbacilli in pure culture (the microbacilli of seborrhea, Sabouraud).

The disease in this simple form is almost noninflammatory and neither itches nor scales; nevertheless, there will be found histologically a progressive hypertrophy of the sebaceous glands and a slowly progressive atrophy of the hair papillae. Seborrhea has definite areas in which it reaches its highest development; on the scalp this area is the vertex, the upper temporal regions and the posterior hair line. The onset of this disease is so insidious, its symptoms so insignificant at first, that the physician is rarely consulted until some complication arouses the patient. Seborrhea is distinctly a disease of the sebaceous follicles; aside from increased oiliness and dilated pores, with alopecia of hairy areas, there is no change in the appearance; no scales nor crusts are present. The disease has its inception at the beginning of puberty, reaches its apogee at the period of sexual maturity, and thereafter retrogresses.

PITYRIASIS SIMPLEX CAPITIS

Pityriasis simplex capitis is a chronic disease characterized by dry, white, dehiscent scales, with only slight inflammatory reaction; in its superficiality, its desquamation, its persistence in a given locality, its slow diffusion, its recurrences after apparent cure and its constant bacteriologic findings, it is similar to pityriasis versicolor. The scales of this disease always show large numbers of a special organism, probably an epidermophyton, which has never been cultivated, discovered by Malassez,[12] called by him a "spore," and to which has been given the name *Pityrosporum malassezii*. (This is Unna's bottle bacillus.) In its pure form, this disease can be most easily studied in children between the ages of 6 and 10. At and after puberty it is sometimes found in combination with seborrhea. More commonly, staphylococcic infection is added, giving rise to the condition known as "dandruff."

This descriptive word, however, is not a synonym, for pityriasis simplex does not itch any more than does pityriasis versicolor. This is to be expected, since both diseases are extremely superficial, and neither causes any microscopic inflammatory reaction. Pityriasis simplex may occur long before the earliest changes of puberty and may be found in full activity in the aged. It produces only a slight, gradual alopecia which can be readily checked by treatment.

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12. Malassez: Notes sur le champignon du pityriasis simple, Arch. de physiol., 1874.

PITYRIASIS STEATOIDES CAPITIS

Pityriasis steatoides capitis is a chronic disease resulting from the proliferation of *Staphylococcus epidermis-albus* (Welch) beneath the scales of pityriasis simplex. Both the spore of Malassez and this staphylococcus are threfore constantly present. The disease is characterized by thicker, yellowish, *apparently* greasy, slightly adherent scales, which on removal leave faintly reddened surfaces, sometimes a little moist. Itching is usually present, and a gradual diffuse loss of hair occurs. In addition to the hyperkeratosis of pityriasis simplex, a slight edema of the underlying epidermis with extravasation of serum and leukocytes is found. The scale, therefore, is no longer a true scale but a "scale crust," consisting of alternate layers of horny cells, microorganisms, leukocytes and dried serum. This sandwich formation of the scale crust is the explanation of its different color and of the feeling of oiliness it gives when rubbed between the fingers.

This condition is dandruff. There is no real excess of fat in the scales, no enlargement of the underlying sebaceous glands; no seborrheic filament can be expressed from the pilosebaceous orifices, and no microbacilli of seborrhea in colonies are found. It is not, then, a seborrhea. The orifices of the oil glands will be found somewhat dilated because the staphylococcic infection has penetrated a short distance into the follicle, but there is no deeper change.

Unna [13] says:

> I have examined sections from fifty-three cases of seborroeic catarrh (from the corpse) mounted in the ordinary method after treatment with osmium (pityriasis cap., so-called seb. sicca, pap. seb. eczema). Of these there were eighteen cases in which the presence of fat in excess could be demonstrated; in nineteen cases there was no fat in the cutis and in the remainder it was only recognizable in small droplets in the cutis.

He also notes the absence of hypertrophy of the oil glands;

> The sebaceous glands are normal and contain their normal amount of fat, but the secretion is dammed up, and is often arranged on the hair, which penetrates the scale, in the form of a layer of fat, and greases it as far as the scale, where it ceases.

Unna's own statistics, therefore, tend to show that in only one third of the cases of dandruff is there an underlying seborrhea—that is, dandruff is not seborrheal though seborrhea may be, and often is, present at the same time.

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13. Unna, P. G.: The Histopathology of the Skin, English trans. by Walker, 1896.

ORGANISMS AS THE CAUSE OF DISEASES OF THE SCALP

It is not the purpose of this paper to champion the germ theory as the sole origin of the conditions discussed. It will be sufficient if the reader will accept the evidence offered by many investigators that different germs are constantly found in great abundance in each of these diseases, and that they vary in number, luxuriance of growth and distribution with such regularity that they may be used for purposes of differential diagnosis with certainty.

In other words, these organisms when found in characteristic numbers and locations are pathognomonic of the disease in which they occur.

It cannot be denied that other factors play an important part; for example, Sabouraud has records of 350 eunuchs only one of whom was bald (and he had universal alopecia).

Hippocratic baldness is unknown in children. It would appear, then, that the influence of the internal secretion of the testes has an important direct or indirect place in the causation of baldness. Heredity also plays a rôle and will be found implicated in many cases of baldness occurring in young men of from 17 to 20. Thyroid exhaustion has been mentioned as a possible causative factor in the baldness of athletes. Mechanical interference with the circulation in the area overlying the occipito-frontalis has been proposed as a cause of alopecia, and the incrimination of intestinal derangement and metabolic disturbances we have always with us.

One may concede or even emphasize these factors, but one must also admit the constant local presence of myriads of organisms found only rarely or in small numbers on normal skins. It is apparent that certain conditions must first be fulfilled in order that these germs may find a suitable soil in which to proliferate. To deny them any part in the course and outcome of the disease process is to take a position difficult to defend when the results of local treatment are considered.

The utility of accepting these organisms as pathognonomic is shown in the following quotation.[5]

> With the edge of a sterile glass slide it is a simple procedure to scrape from the diseased skin either a greasy homogeneous mass, a collection of fatty scales, or a mass of dry scales with, in every case, a few long or short hairs.
>
> This material can be spread on a cover-glass: a double washing with ether removes the fat and prepares the specimen for staining. Simple polychrome blue —or almost any basic dye, is all that is needed for this purpose, and washing with water to remove the excess of stain, and drying is all that is needed to render the slide ready for examination.
>
> One of the following characteristic pictures will be found: (1) A cloudy bluish ground with almost no cellular elements showing numerous groups and myriad units of the small (fin) bacillus of seborrhea. . . . No other bacilli

will be found. This is a pure microbacillary infection. . . . This finding occurs in pure cases of *calvitie* (pure fatty seborrhea). . . . And in cases presenting this picture one can predict a long, tiresome and difficult course of treatment with uncertain or only mediocre results.

(2) In this preparation the material will be found more squamous and less easy to spread and dissociate on the slide. The microscope will show a considerable number of scattered epidermic cells with some grouped into scales and a more complex flora. Always a considerable quantity of the microbacilli of seborrhea will be present, but with them will be found two new and foreign types; the spore bacillus of Malassez (bottle-bacillus of Unna), and a microbe of the staphylococcic type, either singly or in groups. This represents a mixed or hybrid case, pure seborrhea plus pityriasis. . . . With these findings one can predict if not a complete therapeutic success, at least a marked and promptly recognizable amelioration of the disease process.

(3) In the third preparation the cellular elements will be still less easily dissociated on the slide and the microscope will show innumerable horny epidermic cells. No microbacilli of seborrhea will be found but only the cocci previously mentioned and the bottle bacilli (spore bacilli of Malassez).

Here there is no seborrhea, the case is a pityriasis steatoides—the seborrhoeic eczema of Unna. . . . In this case one can give a favorable prognosis, the patient will not become bald and the treatment, even though it may be inconvenient, will be relatively short and give excellent results.

THE BACTERIOLOGY OF PITYRIASIS AND OF SEBORRHEA

Malassez, who first described the organism constantly found in pityriasis simplex, reached the following conclusions:

I. In certain cases of simple pityriasis which I have examined, I have always found microscopic fungi.

II. These fungi consist only of spores, they possess no mycelial tubes. In general these spores are ovoid and budding, more rarely spherical. They are very small; the largest measure 4 or 5 mm. in length and 3 to 3½ mm. in breadth, the smallest being only 2 mm. in their greatest diameter.

III. The fungi in pityriasis are found in the horny layer of the epidermis, they penetrate into the follicles, but not deeply enough to reach the orifices of the sebaceous glands.

IV. They appear to play, in the pathology of pityriasis, the same rôle that other parasites play in those cutaneous affections generally considered to be of a parasitic nature.

V. From this view-point the local treatment of simple pityriasis ought to be essentially anti-parasitic; it should consist of exposing the retreats of the fungi and applying to them parasiticidal agents. This method of treatment has been tried and, when it has been used, has been entirely successful.

This spore was rediscovered by Unna and named by him the "flaschenbacillus." It is known generally by dermatologists of today as the "bottle bacillus." It is polymorphous, and four principal forms are described; (1) spherical, but in different sizes; (2) elongated forms shaped somewhat like a banana; (3) constricted forms, resembling a gourd, and (4) budding forms, recalling those of yeasts. No mycelia

have been found in relation to this organism, and it has never been grown on artificial mediums. This failure to secure a growth in cultures is also true of *Microsporon furfur* of pityriasis versicolor. Sabouraud thinks it belongs among the lower cryptograms, and that it is a fungus belonging to the blastomycetes. Dold thinks it conforms most closely to the classification mycoderma.

The microbacillus of seborrhea (Sabouraud) was found in the comedo by Unna in 1893, was grown by Sabouraud in 1897 and was again studied and described by Gilchrist in 1899. Unna, Horada and Gilchrist considered this organism to be the cause of acne, and Gilchrist named it *Bacillus acnes*. Sabouraud believes it is the cause of seborrhea, acne being the result of a superinfection by staphylococci. Darier says, "Credit is due to Sabouraud for having shown that these microbes, myriads of which exist in the product of fatty seborrhea, belong to a single species, the microbacillus of seborrhoea." He, however, says the growth of this organism is secondary to the seborrhea.

The organism has been so fully described, and its cultural and staining characteristics so thoroughly worked out that repetition is needless. Its acceptance as the cause of seborrhea has not been unanimous, although Sabouraud has shown that it can be found in enormous numbers in every sebaceous filament and in the center of every comedo. It is true that it may be found rather commonly on normal skin but only as isolated units, quite a different thing from a colony. This seems to be the only argument against its acceptance. Certainly it is found in such luxuriance in no other condition. Whether or not one accepts it as the causal agent of seborrhea as distinguished from steatorrhea, it should be accepted as a constant finding in seborrhea, and thus becomes a valuable point in differential diagnosis.

Staphylococcus epidermidis-albus (Welch), Unna's morococcus, Sabouraud's polymorphous coccus with gray cultures, is one of the most common pyogenic organisms found on the skin. Because of its frequence, some dermatologists deny it any causal relation to morbid processes. It is known to be of low virulence and often to be innocuous; therefore, they reason, it cannot be active in any situation. This conclusion seems hardly warranted; it is true that the organism can be readily found by scraping normal skin, but one should remember the large number of awe-inspiring organisms that can be collected from a normal throat before drawing so broad a generalization. For example, one author,[14] speaking of all three organisms under discussion says, "Nor is there the remotest evidence that any of the alleged organisms is specific. All that can be said is that they are found in seborrhea, and

14. Highman, Walter James: Dermatology, New York, The Macmillan Company, 1921.

it may be stated with equal force that they are also found where seborrhea is not."

This is a rather cavalier statement of the argument usually advanced against any attempt to show a causal relationship between any disease and any organism. Sabouraud's answer to such statements is a classic.[9]

On the surface of the healthy skin microbes are rare.

In the first place, it is necessary to establish an important distinction; that between the *isolated microbe* and the *colony*. Isolated units on the skin surface are fairly frequent but colonies of microbes reproducing and multiplying on the skin do not exist, *never exist*, except in visible cutaneous lesions.

We have two methods of proving this statement, both of them absolute. Make a biopsy from clean and normal skin having, for instance, an area of five square millimeters: one may easily then in an entire series of 100 to 200 serial sections which can be cut from this material fail to find a single microbial unit. When one examines two hundred serial sections without finding even one coccus one has reason to think that such a skin is infinitely little microbic.

And when one finds certain wandering cocci, where are they found? At the orifice of a follicle, scattered, one, two, or three without constituting a group active in reproduction, but merely scattered units.

Never does one meet them in the depths of the skin, nor even in the course of a healthy follicle. One finds them, I repeat, in scattered units, each one solitary on the surface of the horny layer. In a biopsy it is not uncommon to find both on the scalp and on the skin series of hair follicles of which even the orifices are sterile and show no microbe whatever.

Another series of experiments tends to corroborate this: one may twenty times in succession, touch a clean skin with a platinum loop and inoculate cultures therefrom without obtaining a single colony.

There is, furthermore, a method of learning the relative number of germs to be found in a scale from the horny layer. That consists in rubbing all its surfaces over a culture tube.

With a squama from normal skin, artificially produced and scraped off one will often fail to secure a single colony, or possibly one, two or three, in rare cases four isolated ones, each developed from one germ. Thus this squama was sterile, or at most, contained three or four micro-organisms. But if the squama is taken from a case of pityriasis of the scalp with fatty scales, many culture tubes inoculated successively will be completely covered with contiguous colonies. . . . . Thus all means of experimentation unite in supporting the . . . . following statements which ought to be clearly understood:

I. The normal skin is infinitely less contaminated than is generally supposed.

II. On the surface of healthy skin one never finds colonies of microbes indicating that their multiplication is taking place *in situ*. The organisms which one finds on the surface of healthy skin are scattered in isolated, living units (cultures will prove this) but are inert (since they remain as single units without forming colonies). . . .

V. In contrast to the almost sterile condition of the normal skin, the pathologic (dechets) débris of the skin: squamae, little crusts, etc., are generally prodigiously infected. And the germs are not found as isolated units, but in colonies, indicating that a large number of organisms have developed around a single germ. . . .

VIII. . . . The epidermis of the healthy skin is normally aseptic and there is no normal cutaneous flora. . . .

What seems most certain is that there is not a human skin on the surface of which one can not find germs, and that the least traumatism augments their chances of multiplication.

In regard to the polymorphous coccus which grows with gray colonies, he says (p. 505):

It is easy and false, it seems to me, to make it the responsible author of any definite dermatosis, and many have not failed to do so; it has been given as the cause of scarlatina (Class 1899) and of eczema (Unna, 1892).

But it seems to me equally easy and false to refuse it, in advance, any importance in any dermatosis. . . . The organism can be found in any form of skin disease just as it can be found on normal skin but in many it is without any influence. Thus one does not find it in the teigne amiantacée of Alibert, even less commonly in psoriasis or the pityriasis rosé of Gibert. They can be found, to be sure, but so rarely that I have searched hundreds of slides of psoriasis before finding one specimen, a single diplococcus, two microbic units.

The coccus with gray cultures, then, is no more the parasite of pityriasis than it is of eczema. It is never the first in any disease and it is the second in all.

I have quoted at length because these statements are, on their face, the conclusions of a scientist who is willing to work to determine the facts and who gives the results of his work as fact, not as opinion. Furthermore, the foregoing quotation must be borne in mind if we are to give Sabouraud's work any consideration.

He believes that there are two basic (mother) diseases to be considered: first, seborrhea—caused by the microbacillus of seborrhea—and second, pityriasis simplex—caused by the spore of Malassez (Unna's bottle bacillus). He believes that these two conditions are entirely distinct, the first being a disease of the sebaceous glands, a comparatively deep, obstinate condition, beginning only with the onset of puberty. The second, in his opinion, has no such connection with puberty, is extremely superficial and is as strictly confined to the horny layer of the skin as is pityriasis versicolor; it is readily amenable to treatment, though prone to recur. Seborrhea produces permanent baldness, and this baldness is almost impossible to prevent. Pityriasis produces a gradual thinning of the hair which may eventually cause baldness, but is easily checked, and the regrowth of hair may be expected. Seborrhea is not essentially a scaling disease. Pityriasis is always a scaling disease.

One may have pityriasis in childhood, and, at adolescence, develop seborrhea. Here we have a combination of two diseases, and the prognosis as to baldness will be that of the more obstinate disease, namely the seborrhea.

Pityriasis simplex makes an extremely favorable breeding ground for the gray staphylococcus (Welch's *Staphylococcus epidermidis-albus*),

and when this secondary infection develops the character of the scales is altered; they become thicker and succulent, give a greasy feel when rubbed between the fingers and are more yellow.

This condition occurs without any change in the sebaceous glands, no hypertrophy, no excess of oil on the surface, no ver·nicelli-like plugs. It is in no way a seborrhea; it is a pityriasis steatoides, or what Thomas Raynald described as the "dandruffe."

COMMENT

We have no new facts to add to this thoroughly muddled subject. We have tried to offer a short statement of the findings of Sabouraud which, it seems to us, are not given their true value in America. Is not his explanation of our clinical experience simpler and more easily taught than the usual textbook statements? Is it not less subject to criticism? Should it not form the basis for the teaching of these common scalp conditions?

THE PRECIPITATION TEST ON SPINAL FLUID IN SYPHILIS *

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Many authors have advocated the use of the precipitation reaction with spinal fluid in the diagnosis of syphilis.

In Kahn's technic,[1] 1 c.c. and 1.5 c.c., respectively, of spinal fluid are placed in each of two test tubes, and to each is then added 0.1 c.c. of dilute antigen. This antigen consists of one part of the antigen which Kahn advocates for use in the precipitation test for syphilitic serum and three parts of physiologic sodium chlorid. The tubes are then thoroughly shaken, and allowed to stand for several hours or until precipitation occurs. He claims favorable results for this method in comparison with the Wassermann reaction and clinical findings. Many workers, among whom are Detweiler,[2] Moody,[3] Ide and Smith,[4] and Grant,[5] have since reported unfavorable results on trying to repeat this work. On the other hand, Anderson and Fisher [6] have reported favorable reactions with a method almost similar to that described by Kahn.

They used 0.6 c.c. of spinal fluid and added 0.05 c.c. of a diluted Kahn's serum antigen. Except for a weaker response in the precipitation reaction, the results paralleled those with the Wassermann test.

I have found that the use of the precipitation test by Kahn's or Anderson and Fisher's methods sometimes gave weakly positive or falsely negative reactions with known syphilitic spinal fluid.

In my method for the precipitation test with spinal fluid, I [7] prepared the antigen in a slightly different manner from those previously suggested.

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* From the Pathological Laboratory of the Roosevelt Hospital.

1. Kahn, R. L.: A Simple Quantitative Precipitation Reaction for Syphilis, Arch. Dermat. & Syph. **5**:570 (May) 1922.

2. Detweiler, H. K.: Kahn Precipitation Test for Syphilis, J. A. M. A. **81**:815 (Sept. 8) 1923.

3. Moody, W. B.: Precipitin Reaction for Syphilis, J. A. M. A. **80**:383 (Feb. 10) 1923.

4. Ide, S., and Smith, G. J.: Comparative Study of Kahn and Wassermann Reactions, Arch. Dermat. & Syph. **6**:770 (Dec.) 1922.

5. Grant, M. S.: J. Lab. & Clin. Med. **8**:468, 1923.

6. Anderson, J. E., and Fisher, E. E.: A Comparison of the Wassermann and Kahn Tests in Three Hundred and Twenty-Nine Cases, New York M. J. & M. Rec. **118**:490, 1923.

7. Ishii, O.: Comparative Studies on the Kahn Precipitation Test for Syphilitic Serum and the Wassermann Test, Arch. Dermat. & Syph. **9**:612 (May) 1924.

Dried beef heart powder was washed five times with about five volumes of ether. The dry powder was first shaken well with the ether and the mixture then centrifugated. The supernatant fluid was poured off and discarded after each centrifugalization. The etherized beef heart powder was then spread out on a glass plate or on paper at room temperature until the odor of ether ceased to be perceptible. This dry ether-extracted beef heart powder was then mixed with five volumes of 95 per cent. alcohol containing 0.5 per cent. cholesterol. Any of the following three procedures could then be carried out: (1) the mixture shaken thoroughly for five minutes at room temperature, (2) the mixture heated for fifteen minutes in a water bath at 54 to 55 C., (3) the mixture heated for twenty-five minutes in a water bath at 37 C. The mixture was then centrifugated for five minutes at moderate speed. The supernatant fluid could be used immediately or at any time thereafter. No deterioration has been observed in one year.

For use with spinal fluid, this stock antigen is diluted with an equal volume of physiologic salt solution. One one-hundredth cubic centimeter of this diluted antigen is added to 0.25 c.c. of spinal fluid, shaken thoroughly for about one minute and then allowed to stand at room temperature until precipitation occurs. The test is set up in duplicate. One should treat as described. In the other, heat the spinal fluid for ten minutes in a water bath at 55 to 56 C. before testing it. In some instances, a more sensitive reaction occurs with the heated spinal fluid, but, in most cases, the better reaction is obtained with the unheated spinal fluid.

PHENOMENA OF PRECIPITATION REACTION FOR SYPHILITIC SPINAL FLUID

When the spinal fluid and antigen are mixed, the fluid is opalescent. A strongly positive fluid shows the presence of fine flocculi in the cloudy fluid within ten minutes after mixing. Those flocculi can readily be made out with the aid of a hand lens. They gradually become larger, and if the tubes are allowed to stand at room temperature for eighteen hours or over night, the flocculi are found clinging to the sides of the test tube and packed on the bottom, while the supernatant fluid is perfectly clear. This can be well brought out if the tube is shaken gently.

With a weakly positive fluid, the supernatant fluid does not become clear, but flocculi remain suspended in the opalescent fluid after standing at room temperature over night.

If no flocculi appear after standing over night, the fluid showing only the original opalescence, the test is negative.

Precipitation and Wassermann Tests on Spinal Fluid Immediately and After Fifty Days

Period tested	Immediately					10 Days Later					20 Days Later					30 Days Later					40 Days Later					50 Days Later				
	Precipitin	Wassermann				Precipitin	Wassermann				Precipitin	Wassermann				Precipitin	Wassermann				Precipitin	Wassermann				Precipitin	Wassermann			
Spinal fluid, c.c.	0.25	1.0	0.5	0.2	0.1	0.25	1.0	0.5	0.2	0.1	0.25	1.0	0.5	0.2	0.1	0.25	1.0	0.5	0.2	0.1	0.25	1.0	0.5	0.2	0.1	0.25	1.0	0.5	0.2	0.1
No. 1	4	4	4	4	2	4	4	4	4	2	4	4	4	4	0	4	4	4	3	0	4	4	4	1	0	..	..	..	..	..
No. 2	4	4	4	4	1	4	4	4	4	0	4	4	4	4	0	4	4	4	5	0	4	4	4	1	0	..	..	..	..	..
No. 3	2	4	4	0	0	2	4	4	0	0	2½	4	4	0	0	3	4	4	0	0	3	4	2	0	0	3	4	2	0	0
No. 4	1	4	3	0	0	1	4	2	0	0	1	4	2	0	0	1	4	2	0	0	1	4	2	0	0	1	4	2	0	0
No. 5	2	4	4	4	2	2½	4	4	2	0	2½	4	4	2	0	2½	4	4	0	0	2½	4	3	0	0	2½	4	2	0	0
No. 6	2	4	4	0	0	2½	4	4	0	0	2½	4	4	0	0	2½	4	4	0	0	2½	4	4	0	0	2½	4	4	0	0
No. 7	1	4	3	0	0	1½	4	1	0	0	1½	4	0	0	0	1½	4	0	0	0	1½	3	0	0	0	1½	3	0	0	0
No. 8	2½	4	4	3	0	2½	4	4	2	0	2½	4	4	2	0	2½	4	4	2	0	..	..	..	..	..	..	..	..	..	..
No. 9	2	4	0	0	0	2	3	0	0	0	2	3	0	0	0	2	3	0	0	0	..	..	..	..	..	..	..	..	..	..
No. 10	1	4	1	0	0	1	3	0	0	0	1	0	0	0	0	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

The figures show the degree of the reaction: 4 indicates ++++; 3 indicates +++, etc., and 0 negative.

The flocculi obtained with spinal fluid are not so large as those obtained with serum, and it is advisable to use a hand lens in the examination of the tests.

A COMPARISON OF PRECIPITATION REACTION WITH FRESH AND OLD SPINAL FLUIDS

In the experiments summarized in the table, the spinal fluid up to three days after their withdrawal from the canal gave precipitation reactions which were almost identical with the results obtained after preserving the fluid at icebox temperature for from ten to fifty days. In a few instances, slightly stronger reactions were obtained with the older fluids, while the Wassermann tests were identical or weaker in old than in fresh fluids.

The Wassermann test was that of the sheep cell system. Spinal fluid doses were 1, 0.5, 0.2 and 1.01 c.c., respectively. To each of these tubes was added 1 c.c. of a dilution of 1 : 60 of 0.4 per cent. of cholesterolized 95 per cent. alcoholic beef heart extract and 1 c.c. of a dilution of 1 : 20 to 1 :25 of guinea-pig complement as two units, and then they were incubated for fifty minutes in the water bath at 37 C. In another set, each tube received 1 c.c. of a dilution of 1 : 20 of plain alcoholic extract of beef heart antigen and complement, and was then kept for four hours in the icebox. Both sets then received 2 c.c. of sensitized sheep cells which contained 1.5 units of amboceptor, and they were then placed in the water bath at 37 C. for fifteen minutes. The readings were made soon after this final incubation.

The sensitized sheep cell mixture was prepared by mixing 1 c.c. of 4 per cent. suspension of sheep cells with amboceptor, so that 1 c.c. represents 1.5 units of amboceptor. The mixture was allowed to stand at room temperature for fifteen minutes before using for the reaction.

Comparison of the precipitation test with the Wassermann test and the colloidal gold reaction in spinal fluid is here described, showing close agreement between all three methods.

XXXVIII.—A CASE OF YAWS OCCURRING IN MISSOURI *

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This case of yaws, which apparently had its origin in St. Louis, is reported because of the rarity with which yaws occurs endemically in the United States. Fox [1] reviewed the literature and reported a case in 1922. He mentions altogether fifty-one cases, the majority of which were not fully described or formally reported. Most of the cases were discovered in the northern seaports, and, presumably, were imported from foreign countries. Subsequent to Fox's article, a case has been reported in California by Alderson and Coe.[2] Only twenty such case reports may be found in the literature. During 1922, Moss and Bigelow [3] reported on 1,046 cases in the Dominican Republic. Gutierrez [4] reported on the treatment of 275 cases with neo-arsphenamin in the Philippine Islands. Many other similar reports may be found by reference to any standard index of bibliography.

REPORT OF A CASE

History.—A colored man, aged 27, unmarried, was admitted to the Barnes hospital, Jan. 5, 1923, complaining of sores on the skin and itching. His family history was irrelevant. He had had measles, mumps, smallpox and whooping cough during childhood. Otherwise he had been healthy up to the present illness. He denied venereal infection (his mistress had a + + + Wassermann reaction of the blood). He was born in Tennessee, and never left there until during the war when he was stationed at Camp Meade, Md., for two weeks. On being discharged from the army the patient visited in Cairo, Ill., for three months. He had been in St. Louis for the past two years, working in a packing plant, where he was in close contact with cattle and hides. The onset occurred

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* Studies, observations and reports, from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

1. Fox, H.: Prevalence of Yaws (Frambesia Tropica) in the United States, Arch. Dermat. & Syph. **6**:657 (Dec.) 1922.

2. Alderson, H. E., and Coe, H. C.: Report of a Case of Yaws in California, Calif. M. J. **21**:162, 1923.

3. Moss, W. L., and Rigelow, G. H.: Yaws: An Analysis of 1,046 Cases in the Dominican Republic, Bull. Johns Hopkins Hosp. **33**:43, 1923.

4. Gutierrez, P. D.: Yaws: Its Manifestation and Treatment by Neo-Arsphenamin, Arch. Dermat. & Syph. **6**:265 (Sept.) 1922.

three months before admission, with small nodular lesions in front of the left ear, which the patient stated looked like warts. These gradually increased in size, became harder, and were covered with white scales. He treated them with a plaster, and the lesions became raw and bloody. The patient then came to the outpatient department, two months before admission for treatment. At this time there was a lesion about the size of a twenty-five cent piece, fungating and

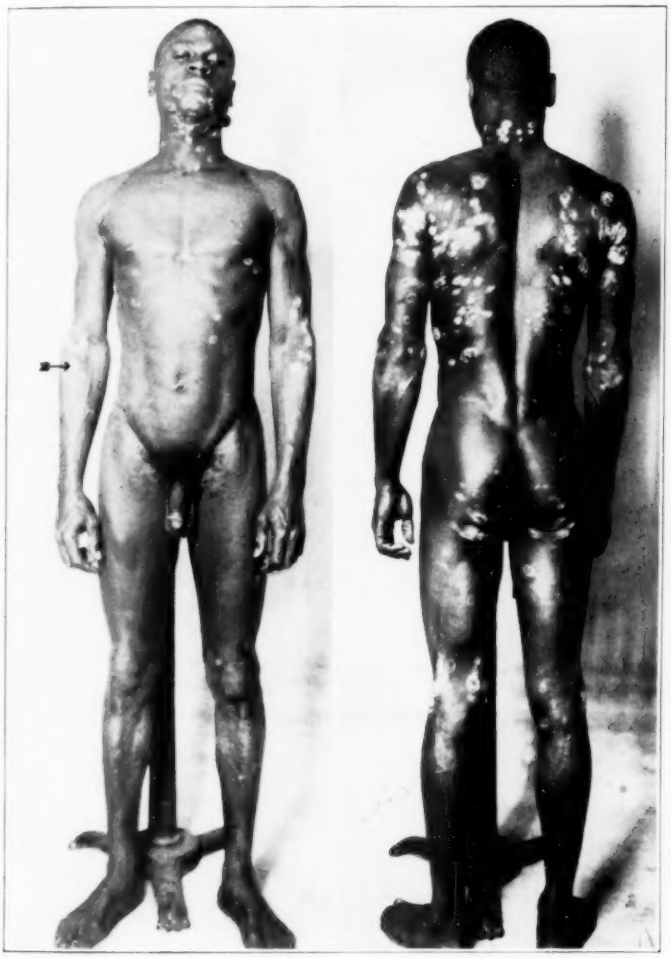

Fig. 1.—Lesion marked with arrow excised for study.

ulcerating, and the only lesion present. The patient also used some "SSS Blood Medicine," which he purchased at a drug store. Two weeks before admission he noticed the appearance of papules on the neck, face, arms, abdomen, back and legs. These were hard, smooth and slightly elevated. They gradually increased in size and became covered with white scales. There was considerable pruritus. A lesion also developed on the hard palate.

Physical Examination.—This was negative, except for the skin condition and pyorrhea alveolaris. The skin eruption was generalized, with a more or less selective distribution, as shown in Figure 1. The primary lesion was a nodule varying in dimension from 0.3 to 2 cm. The other nodules occurred in groups and in circinate arrangement. Where the circles of nodules contained a great many individual lesions, a plaque of granulomatous tissue was formed. The circinate lesions and the plaques were distinctly grouped. They were thickest

Fig. 2.—Lesions in various stages of development on posterior surface of right shoulder.

over the scapular and subscapular regions, and in the posterior surface of the shoulders and upper arm, the lower half of the buttocks, at the external surfaces of the knee joints, the anterior surfaces of the elbow joints, anterior axillary folds, chin, forehead and neck, both anteriorly and posteriorly. The primary nodule above described was practically the same color as the skin. There was some infiltration, but not the amount usually seen in syphilis. They were elastic to the touch. The surface of many of the plaques and groups was covered with grayish, somewhat tenacious scales (Fig. 2). Behind the right ear and also in front and above the left ear were granulomatous, nonulcerating, healing plaques

about 3 cm. in diameter. When the patient was first seen two months before admission to the hospital, these plaques were fungating and ulcerating and were the only lesions present. On the hard palate, just posterior to the teeth, was an ulcerated area 2.5 cm. in diameter.

Laboratory Data (Jan. 6, 1923).—The findings on this date were: red blood cells, 5,200,000; white blood cells, 6,600; hemoglobin, 85 per cent.; differential count: polymorphonuclears, 62.5 per cent.; polymorphonuclear eosinophils, 1 per cent.; polymorphonuclear basophils, 1 per cent.; lymphocytes, 33 per cent.; large mononuclears and transitionals, 2.5 per cent.; blood Wassermann test +++ (+); Kahn test, +++ (+); prostatic secretion, few clumps of pus, otherwise negative. Urinalysis: turbid, straw-colored urine; specific gravity, 1.032; acid reaction; albumin, trace; no sugar. Microscopic examination

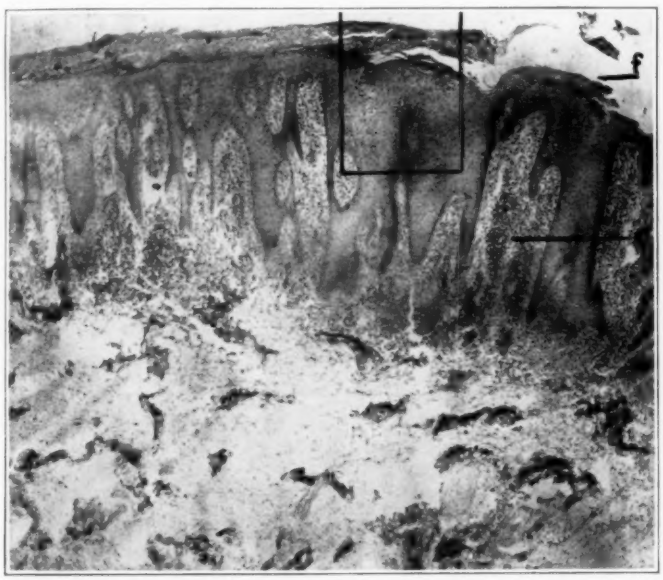

Fig. 3.—Low power magnification of section of lesion, alcohol fixation, stained with Goodpasture's polychrome methylene blue; *f*, crust; *c*, leukocytic infiltration. Section shows extent of proliferation of rete pegs, edema of corium and epithelium, etc.

revealed few white blood cells and epithelial cells, an occasional hyaline cast, no red blood cells; phenolsulphonephthalein, 35 per cent. for two hours. The temperature was 37 C. (98.6F.); the pulse rate, 84; respiration, 20.

A roentgenogram of the distal end of the radius, ulna, carpal bones, lower end of humerus and bones of the feet showed a very coarse articular structure.

Treatment and Course.—On Jan. 13, 1923, a somewhat regressing lesion (Fig. 1) from the volar surface of the right forearm was excised under procaine, 2 per cent., and epinephrin anesthesia, for diagnosis. Half of the specimen was macerated and injected into rabbit testicles and into the eyebrow of a macacus rhesus monkey. An occasional spirochete was seen in the macerated material. Five days later, a lesion on the back of the neck was infiltrated with physiologic

sodium chlorid and the entire epithelial covering shaved off down to the middle of the dermal layers. This material was emulsified in physiologic sodium chlorid and injected into rabbit testicles. Dark-field examination was negative. Repeated dark-field examinations on ten other widely separated lesions were

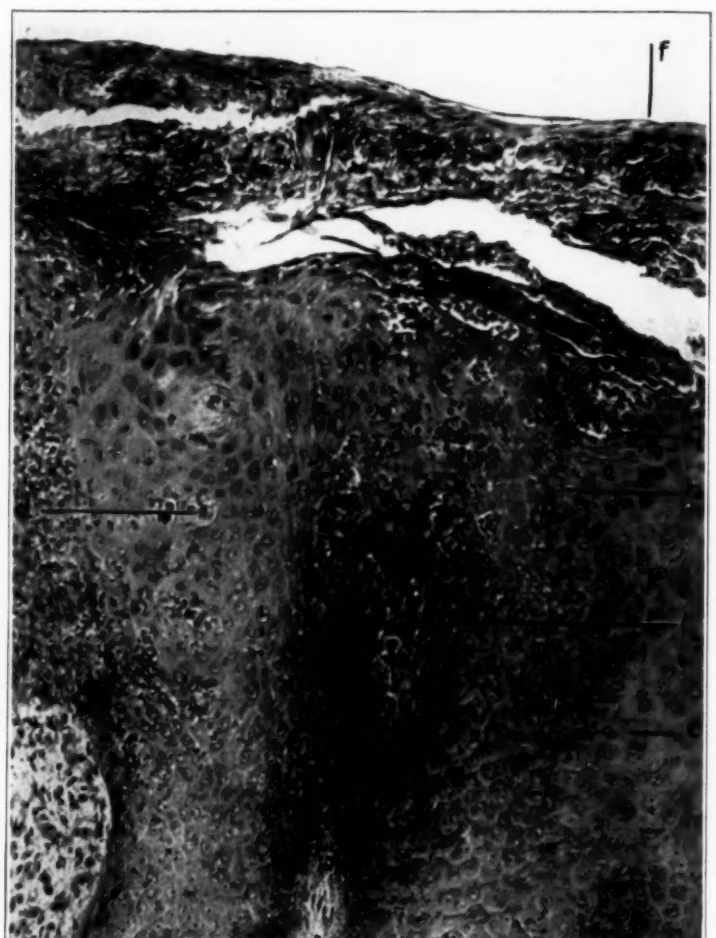

Fig. 4.—Higher power magnification of marked portion of Figure 3, *a*, *d*, miliary abscesses; *b*, nucleus separated from protoplasm; *c*, diffuse leukocytic infiltration; *e*, edematous epithelial cells.

negative. Immediately following this examination, 0.45 gm. of neo-arsphenamin was given intravenously. The next day, the lesions began to show signs of regression.

January 22, 0.45 gm. of neo-arsphenamin was given intravenously. The lesions were elevated about one fourth as high as at the time of the previous injection.

January 24, 0.6 gm. of neo-arsphenamin was given intravenously.

January 28, the lesions were now macular and deeply pigmented. The skin was in general smoother and shiny. The patient's general appearance was much improved.

January 29, 0.9 gm. of neo-arsphenamin was given intravenously. The patient was discharged from the hospital on Jan. 31, 1923. The skin was smooth and shiny everywhere. The sites of the lesions were marked by faint rashes and scaly areas.

February 8, the blood Wassermann test with cholesterolized antigen was +++ (+); noncholestrinized, ++. Nine-tenths gram of neo-arsphenamin was given intravenously.

February, 18, the blood Wassermann test was negative with both antigens. April 13, 1923, the blood Wassermann test was negative with both antigens.

Microscopic Findings.—Low power examination of the skin sections (Fig. 3) revealed a sharply circumscribed area in which the epidermis was markedly thickened, with tremendous elongation of the rete pegs. The surface of the lesion was covered with crusts. The corium was markedly edematous, and there was a rather diffuse leukocytic infiltration which involved both the corium and the epithelial layers. Examination under higher power (Fig. 4) revealed diffuse and sharply circumscribed areas of infiltration in the epithelium, with polymorphonuclear leukocytes, mononuclears, both large and small, and plasma cells. The diffuse infiltrations were made up of mononuclear cells. Sharply circumscribed miliary abscesses, filled for the most part with polymorphonuclear cells, occurred in all portions of the epithelial structures, although occurring in greater numbers nearer the surface than near the basal layers. The crusts were made up of the products of hyperkeratosis and exudate. The epithelial cells showed signs of degeneration. They were edematous, and many of the nuclei were separated from the protoplasm. Perivascular infiltration was found in the corium, but not to the extent seen in syphilis. The Levaditi sections did not show the presence of *Spirochaeta pertenuis* in any portion of the sections. This, of course, may possibly be due to the fact that the lesion studied was regressive.

EXPERIMENTAL WORK

A skin lesion about 2 by 3 by 0.4 cm. was removed from the upper part of the volar surface of the right forearm under local anesthesia of 2 per cent. procain containing 1:5,000 epinephrin chlorid. The lesion was cut in half longitudinally and one half used for sectioning by the paraffin method and study by Levaditi's hematoxylin and eosin, and Goodpasture's methylene blue stains. The other half was cut up into small bits with sterile scissors and macerated in a warm sterile mortar. Warm sterile physiologic sodium chlorid was used as the diluent in the maceration process. Dark-field examinations were repeatedly made on the emulsion, but only two nonmotile spirochetes were seen. The lesion emulsion was injected into animals within thirty minutes after removal, as shown in the table. Some of the patient's venous blood was injected into rabbits. These rabbits had a severe temperature reaction, but otherwise were not effected. Two days later dark-field examinations were made on ten different lesions on the patient. No spirochetes were found. A lesion about 1.5 by 1 by 0.3 cm. contiguous to the spinous process of the seventh cervical vertebra was put under pressure anesthesia by thoroughly infiltrating the surrounding skin with sterile physiologic sodium chlorid. The top of this

Experimental Data

Animal	Number, Sex	Material Injected	Period Observed	Lesions	Blood Wassermann Test	Site of Injection	Disposal
Monkey... (Rhesus macacus)	Male	1 c.c. macerated lesion	20 weeks	None	Negative	Left eyebrow	Discarded
Rabbits...	355 Male	1 c.c. macerated lesion	2 weeks	None	.....	Right testicle	Killed
	386 Male	1 c.c. macerated lesion	20 weeks	None	Negative	Right testicle	Discarded
	389 Male	1 c.c. macerated lesion	8 weeks	None	.....	Right testicle	Died; pneumonia
	390 Male	1 c.c. macerated lesion	11 days	None	.....	Right testicle	Died; pneumonia
	394 Female	2 c.c. macerated lesion	20 weeks	None	Negative	Mammary gland	Discarded
	476 Male	2 c.c. macerated lesion	5 weeks	None	.....	Right testicle	Died; pneumonia
	477 Male	2 c.c. macerated lesion	20 weeks	None	Negative	Right testicle	Discarded
	478 Male	2 c.c. macerated lesion	3 weeks	None	.....	Right testicle	Died; pneumonia
	474 Male	1 c.c. fresh lesion	20 weeks	None	Negative	Right testicle	Discarded
	473 Male	1 c.c. fresh lesion	20 weeks 21 weeks 22 weeks	None	+ + + + + — — — — — — —	Right testicle	Discarded
	395 Female	5 c.c. blood	20 weeks	None	Negative	Intravenously	Discarded
	475 Female	3 c.c. blood	20 weeks	None	Negative	Intravenously	Discarded
	396 Female	3 c.c. blood	20 weeks	None	Negative	Intravenously	Discarded

lesion was scraped off with a sharp scalpel well down into the corium, and the substance of the lesion was emulsified and injected into rabbits. Only one of all the rabbits used showed any signs of yaws; that is, a positive Wassermann reaction. No testicular or other lesions developed.

SUMMARY

The author describes a case of yaws occurring in a young negro who probably became infected while in St. Louis, possibly from his work or from his mistress. Biologic and microscopic studies were made from an excised lesion. The patient promptly recovered under neo-arsphenamin therapy.

XXXIX.—THE INCIDENCE OF SYPHILIS AT THE WASHINGTON UNIVERSITY DISPENSARY AND ITS RELATIONSHIP TO ECONOMIC CONDITIONS *

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AND
ADOLPH H. CONRAD, M.D.
ST. LOUIS

In 1920, C. Morton Smith,[1] in a paper read before the American Dermatological Association, made the statement that "It seems probable that secondary and tertiary lesions of syphilis will continue to occur less and less frequently." In the discussion on this paper, various observers agreed with him in this and also in the observation that teaching material was becoming more scanty. The belief seems to have been that acute syphilitic eruptions were gradually diminishing in numbers, and that teaching material would eventually become so scarce as to constitute a serious handicap for future students of medicine.

At that time it was our impression that a similar state of affairs obtained at the Washington University Medical School. We then began gathering the material for this statistical study. It seemed wiser, however, to wait a little longer and to include the years 1921 and 1922 in order to observe postbellum effects, if any. During the course of the work, it was found feasible to enlarge the scope somewhat, and the results are presented herewith in the form of a table and nine charts.

In order to have a true picture of the incidence of the various types of syphilis in the clinic population, all of the charts, with the exception of Chart 1, are constructed on the basis of cases per thousand new cases (all diseases) admitted to the dispensary. The classification used was that of Engman.[2]

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* Studies, observations and reports from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

1. Smith, C. Morton: The Vanishing Lesion: A New Problem in Teaching, Arch. Dermat. & Syph. **2**:639 (Nov.) 1920.

2. Weiss and Conrad: The Medical and Social Care of Syphilis at the Washington University Dispensary, Am. J. Syphilis **4**:275 (April) 1920, Appendix D.

COMMENT

In the period 1915 to 1922, inclusive, 142,096 new patients (all diseases) were admitted to the Washington University Dispensary. In the same period, 4,489 patients with syphilis were admitted. Therefore the incidence of syphilis in the clinic population, as near as it can be figured, was 31.59 cases per thousand.[3] In this same period, 1,544 patients with latent syphilis were admitted, or 34.4 per cent. of the total number of patients with syphilis. Two thousand, three hundred

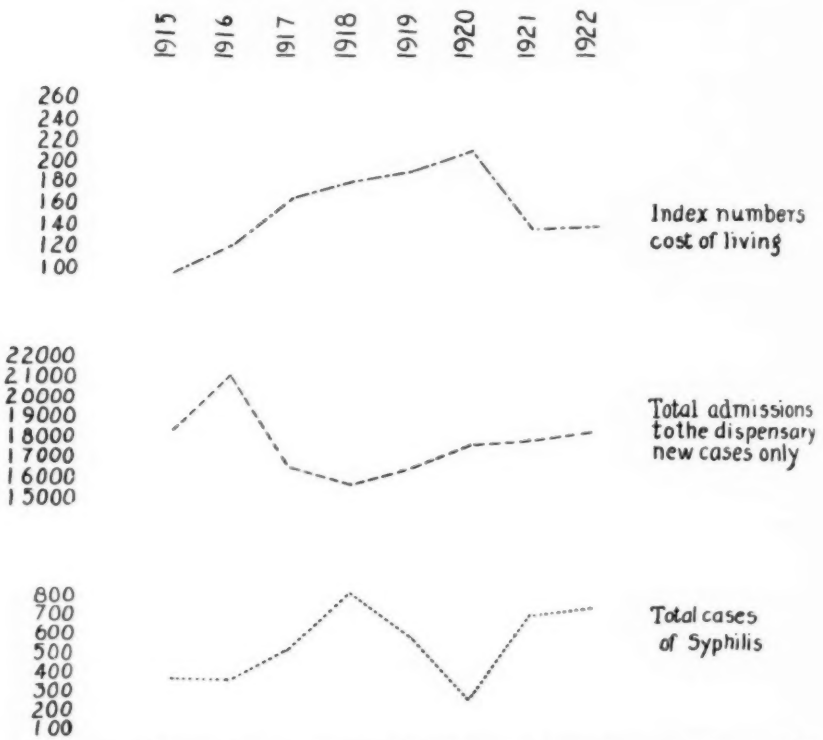

Chart 1.—Comparison of curves showing total number of patients with syphilis, total number of new patients (all diseases) admitted to the Dispensary, and the average index numbers of the cost of living.

and eight patients with skin syphilis were admitted (primary, early and late) or almost one half of the total number of cases of syphilis, an average of about 300 cases a year. The total of neurologic cases was 404, or 9 per cent. of the total number of cases of syphilis.

There was a gradual increase in all cases of syphilis, culminating in a high point in 1918 (mobilization of troops completed). It is difficult to explain this rise as an effect of the war, as one would expect

3. Congenital syphilis is not included in this study.

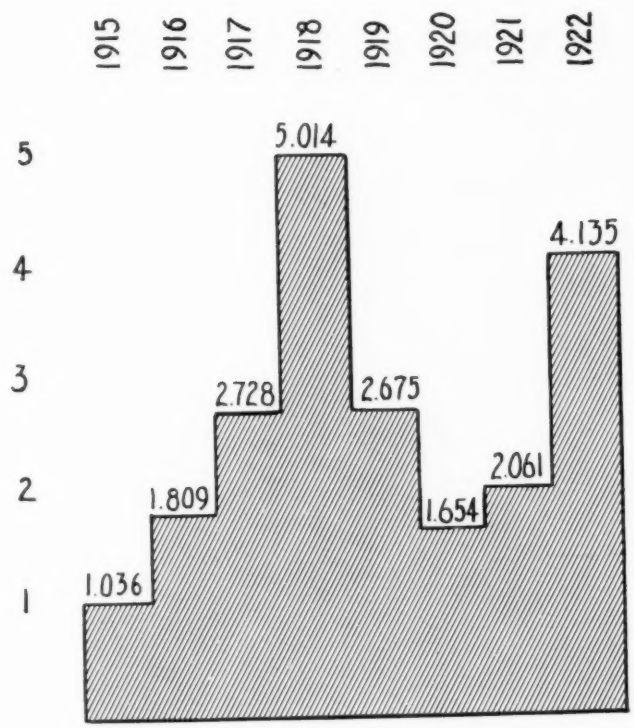

Chart 2.—Primary syphilis; number of cases per 1,000 new cases.

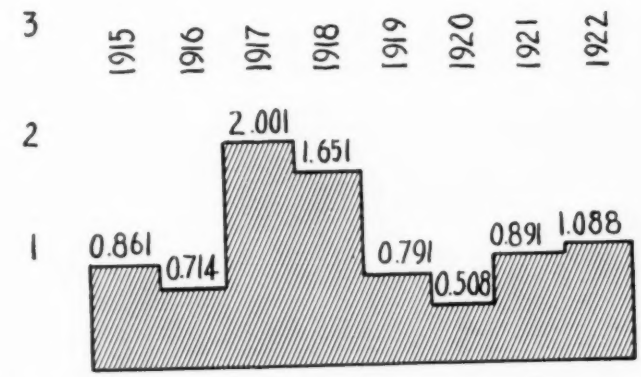

Chart 3.—Macular syphilis; number of cases per 1,000 new cases.

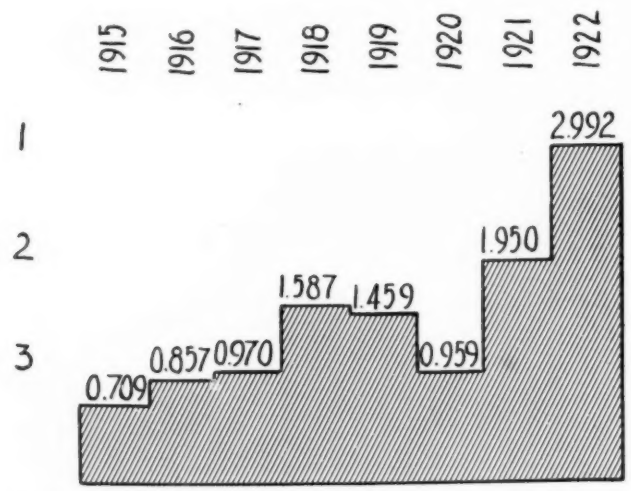

Chart 4.—Papular syphilis; number of cases per 1,000 new cases.

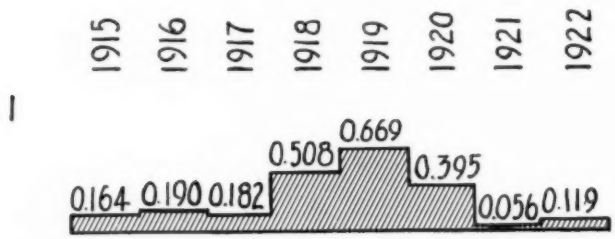

Chart 5.—Pustular syphilis; number of cases per 1,000 new cases.

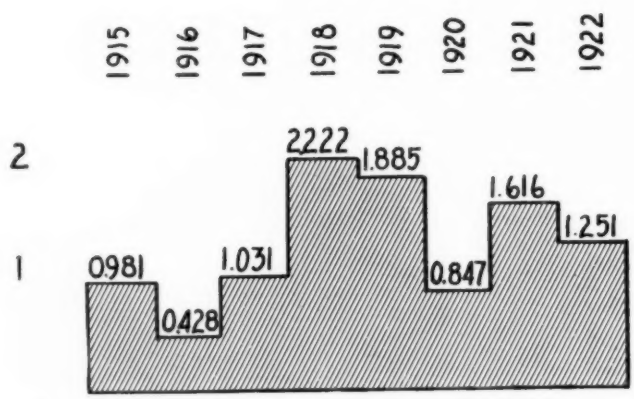

Chart 6.—Nodular syphilis; number of cases per 1,000 new cases.

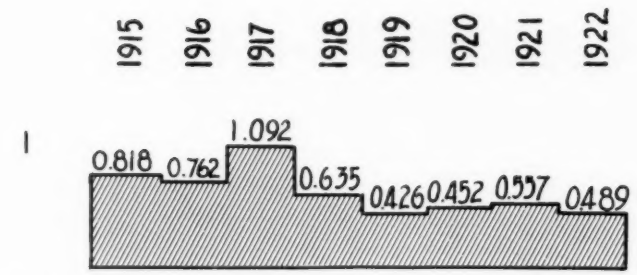

Chart 7.—Squamous syphilis; number of cases per 1,000 new cases.

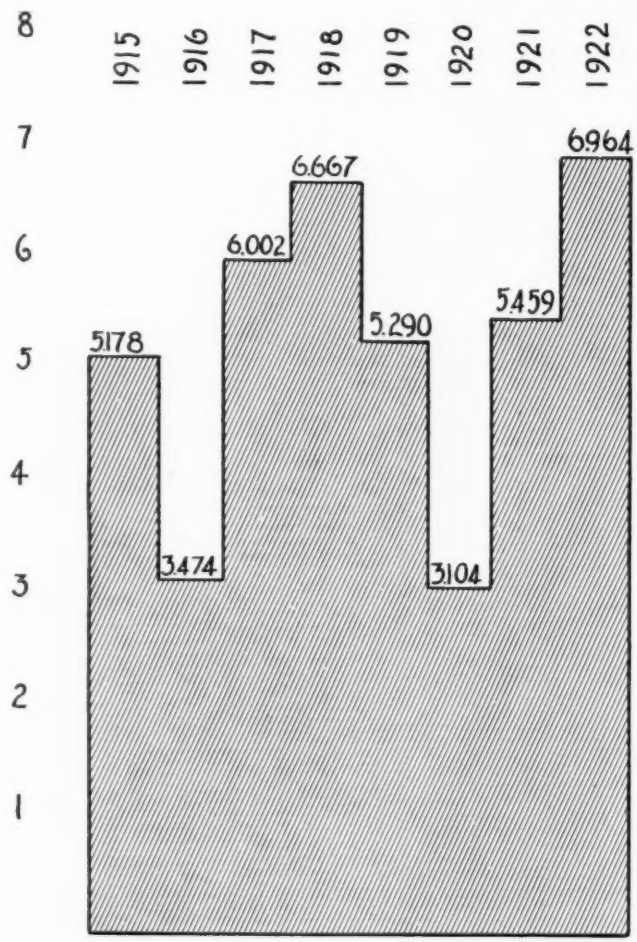

Chart 8.—Gummatous syphilis; number of cases per 1,000 new cases.

that the incidence of syphilis in the civil population would fall as the younger men were withdrawn from civil life (Chart 1). However this same striking rise is seen in primary syphilis (Chart 2), in gummatous syphilis (Chart 8) and in neurosyphilis (Chart 9), all of the types that are usually quite obvious to the patient. In 1918, the dispensary had the fewest new cases (all diseases) in eight years, and the cost of living had gone far more than half way toward its high point; therefore, when the dispensary admissions for all disease were

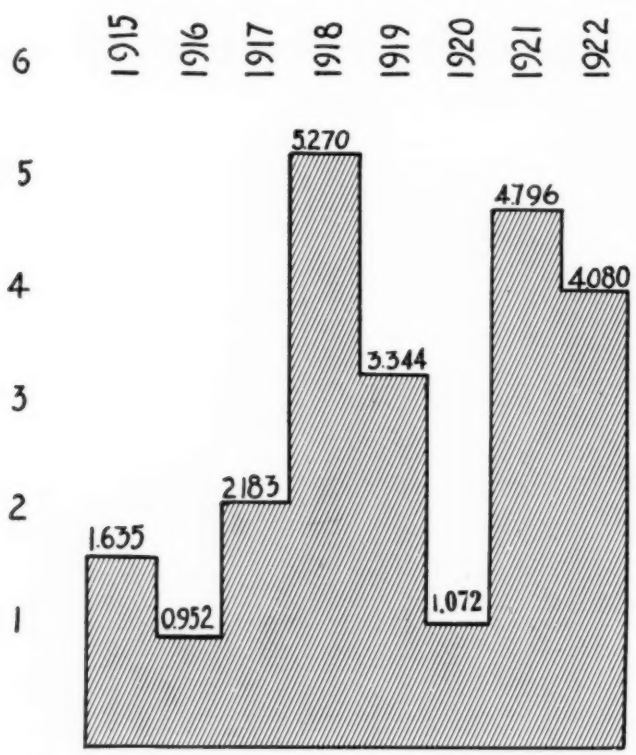

Chart 9.—Neurosyphilis; number of cases per 1,000 new cases.

lowest, the number of patients admitted for syphilis was highest. Some of the factors involved, we believe, were the campaigns against venereal disease, the physical examinations of the draft and an actual increase in the syphilitic population due to war time conditions.

Chart 1, then, shows a decrease in 1919 (demobilization) and a further decrease in 1920 (demobilized). There was again an increase in numbers in 1921 and 1922, and it is our impression that 1923 will show equal or greater figures than 1918. A factor of no little importance in this more recent increase is the growth of the negro population of St. Louis due to disturbed economic conditions in the South, and

emigration of the negroes to the North. It has been estimated by the Urban League of St. Louis that from 35,000 to 40,000 negroes have entered St. Louis in the last twenty-two years, to become more or less permanent residents. A large part of this increase occurred in the last four years, the secretary of the Missouri Negro Industrial Commission reporting [4] that the negro population of Missouri has probably increased by 20,000 since the last census.

In 1918, there were eighty-three cases of nerve syphilis. This figure dropped to nineteen in 1920. Then there was a remarkable rise to eighty-six in 1921, and seventy-five in 1922

With demobilization of the troops, there was a decided fall in all types of syphilis, followed by an abrupt rise two years later. This rise was in all types, but it is particularly noticeable in early syphilis and in nerve syphilis.

An attempt was made to secure figures on unemployment for the St. Louis Industrial District from 1915 to 1923. We were unsuccessful in securing reliable figures, and hence were unable to construct a chart. It is, however, a matter of common knowledge that as the cost of living increased from 1915 to 1920, unemployment decreased. Therefore in 1920, when the cost of living was at its highest point, we had the least unemployment; at this time, we had the fewest patients with syphilis admitted to the dispensary. If we took this fact at its face value we should be inclined to think that as unemployment decreased, the incidence of syphilis decreased. That this is probably not the case is shown by our own and our colleagues' experience in private practice. We treat many more patients with syphilis in our offices when most men have work. The point is, then, that when the people as a whole are well supplied with money, they do not come to the clinic for the treatment of syphilis; therefore, the clinic morbidity rate falls.

With deflation beginning in 1920, there was a fall in the cost of living and a rise in unemployment; so we see a sharp rise in the clinic morbidity rate, and we experienced a fall in the number of private cases of syphilis.

Many factors, such as education of the public, better methods of diagnosis, the more universal availability and use of diagnostic methods, including lumbar puncture, are involved in attempting to arrive at the basic laws governing the rise and fall of venereal disease morbidity rates.

It is to be noted that we now have sufficient teaching material in our clinic. We believe, however, that the type of syphilitic eruption is slowly changing, as we see exceedingly few profuse generalized erup-

4. St. Louis Star, Dec. 29, 1923.

tions, but comparatively many mild or milder generalized eruptions. We see but few deep destructive gummatous lesions and comparatively many mild gummas.

Is the virulence in general of the spirochete on the decrease, or is a gradual racial immunity being developed? Many years must elapse before this question can be answered, but to us the trend seems to be in the direction of racial immunity. Certain it is that little malignant syphilis is now to be seen, whereas in the early years of its spread malignancy was the rule.

As to the late central nervous system and vascular effects, the trend seems to be in the direction of an increase. Whether this is actual or only relative, we are at present unable to state. We are inclined to think that this increase is only relative.

SUMMARY

A table and a series of charts are presented showing the incidence of syphilis and of the types of syphilis at the Washington University Dispensary.

All Patients with Syphilis Admitted to the Dispensary from 1915 to 1923, Showing Various Types by Years and the Totals. Congenital Syphilis Is Not Included.

	1915	1916	1917	1918	1919	1920	1921	1922	Totals for Eight Year Period
Total new cases admitted to dispensary	18,346	21,011	16,494	15,750	16,446	17,718	17,951	18,380	142,096
Primary	19	38	45	79	44	29	37	76	367
Macular	16	15	33	26	13	9	16	20	148
Papular	13	18	16	25	24	17	35	55	203
Pustular	3	4	3	8	11	7	1	2	39
Total early*	36	48	60	90	73	34	89	153	583
Latent	125	84	157	250	229	114	309	276	1,544
Nodular	18	9	17	35	31	15	29	23	177
Squamous	15	16	18	10	7	8	10	8	92
Gummatous	95	73	99	105	87	55	98	128	740
Total late†	162	136	215	240	193	116	137	159	1,358
Tabes	15	7	23	25	28	19	15	15	138
Paresis	5	6	2	3	4	3	26	6	55
Taboparesis	0	3	5	25	14	4	2	1	54
Meningovascular	3	2	0	4	2	0	43	53	107
Total neurologic§	30	20	36	83	55	19	86	75	404
Total, all types¶	380	381	529	816	608	315	703	747	4,480¶

* Includes cases diagnosed as early syphilis, but type not specified.
† Includes cases diagnosed as late syphilis, but type not specified.
§ Includes cases diagnosed as central nervous system syphilis, but type not specified.
¶ Includes cases diagnosed as syphilis, but stage and type not specified.

The charts and table show an ebb and flow in the tide of syphilitic morbidity which is apparently related to economic conditions.

The syphilitic morbidity rate at the Washington University Dispensary varies inversely with the number of people gainfully employed in the St. Louis industrial district.

The basic law governing the syphilitic morbidity rate in general cannot be stated, and, until more universal reporting of venereal disease to the health authorities comes into practice, this basic law will probably not be found.

That there is, however, an ebb and flow in the tide of syphilitic morbidity should always be taken into account by those who are studying morbidity rates of venereal disease, and especially by public health officers who are attempting to arrive at conclusions regarding the value of laws compelling the reporting of these diseases.

STUDIES IN IMMUNITY IN RINGWORM INFECTIONS

II. ACTIVE INDUCED IMMUNITY *

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In the literature, there are diverse views concerning the induction of an active immunity against ringworm in both man and the lower animals. This, to some degree, appears to depend on variation in the antigenic substance (simple vaccines, fungus extracts) used by the various experimenters.

Aside from its academic interest, this question of an active induced immunity involves two important clinical problems, namely, prophylaxis and treatment. Of the two, that of treatment appears to be the most important, since it is almost always possible, at least in institutions, to isolate infected children, the common sufferers with ringworm, particularly of the scalp. From the standpoint of treatment, the divergence of opinions concerns the ability of these authors to induce an active immunity not only in deep but also in superficial ringworm infections. It should be noted, however, that the majority are in more or less agreement respecting the value of these substances in deep ringworm. For superficial ringworm of the scalp, we know definitely that depilation with the roentgen ray, the fall of hair carrying the fungus with it and therefore not an immunizing process, is the means of cure par excellence. Unfortunately, this mode of therapy is not universally applicable, as when the child is excessively nervous or too young, and in either case does not cooperate. It is obvious that, in these types, our ability to induce an active immunity would be of decided value.

LITERATURE

Bloch and Massini [1] used a fungus extract (tricophytin) to cure deep tricophytosis, with, according to these authors, good results; but in superficial ringworm, their results were negative, as were those of the originator of tricophytin (Plato) and of a subsequent investigator, Truffi.[2] Bloch,[3] who is a strong supporter of the use of tricophytin,

* From the Research Institute for Cutaneous Medicine, Philadelphia, Pa.

1. Bloch, B., and Massini, R.: Ztschr. f. Hyg. u. Infectionskrankh. **65**:68, 1909.

2. Truffi, M.: Recherche sulla, trichophytins, Clin. med. ital. **43**:377, 1904.

3. Bloch, B.: Ann. de dermat. et syph. **2**:1 and 2 (Jan. and Feb.) 1921.

administers it constantly in his clinic in the cure of deep ringworm. Scholtz [4] did not obtain striking results with Höcht's tricophytin in superficial ringworm. Fuhs,[5] using a different type of tricophytin, that of Joannevics (prepared by digestion of cultures), claims to have obtained superior results, and, I believe, with reason, in the treatment of deep ringworm by subcutaneous injections of from 0.02 c.c. to 0.05 c.c. every third day.

Strickler [6] reports that he has obtained good results in superficial ringworm with simple fungus vaccine. Engman and McGarry [7] reported two cases of sycosis parasitica (deep form?) treated and cured with this vaccine. On the other hand, Lavinder,[8] without drawing final conclusions, has a distinct recollection that his laboratory and clinical staff were not greatly impressed by the results obtained with it, and Whitfield's results in four cases, quoted by Pusey,[9] were entirely negative.

That certain of the ringworm organisms, under proper conditions, produce toxins, is a clinical (tricophytides, probable production of immunity in deep ringworm) and an experimental fact.[10] From the standpoint of induced immunity, are only the toxins necessary, as is the case for example with the Klebs-Loeffler bacillus(the results in human subjects claimed by some of the foregoing authors with tricophytin would appear to indicate this), or do the organisms alone suffice (results with simple vaccines), or are organism and toxin both necessary for the production of a maximum immunity?

Despite the alleged clinical results of some investigators, it appears definitely established that the use of the toxins alone, in the form of fungus filtrates, does not cause the production of immune bodies, at least in detectable amounts, or in amounts sufficient to prevent inoculation "takes" or to shorten the course after "take" has occurred in animals or to be of clinical use in the cure of superficial ringworm in the human subject. With simple vaccines, the evidence is inconclusive either way.

Bloch [1] was not able to induce immunity against ringworm in guinea-pigs by repeated injections of Plato's phytin, although we have

4. Scholtz, W.: München. med. Wchnschr. **65**:509, 1918.

5. Fuhs, H.: Wien. klin. Wchnschr. **33**:653 (July 22) 1920.

6. Strickler, A.: The Vaccine Treatment of Ringworm of the Scalp, J. A. M. A. **65**:224 (July 17) 1915.

7. Engman, M., and McGarry, R. A.: Two Cases of Trichophytosis Barbae Cured by the Use of Strickler's Ringworm Vaccine, J. A. M. A. **68**:543 (Feb. 17) 1917.

8. Personal communication.

9. Pusey: Principles and Practice of Dermatology, Ed. 3, New York, D. Appleton & Company, 1917, p. 122.

10. Greenbaum, S. S.: J. Infect. Dis. **31**:26 (July) 1922.

already shown (Paper 1) that a partial general immunity, both straight and crossed, can be obtained by the subcutaneous injection of living suspensions of *Achorion quinckeanum*, *Microsporon lanosum* and *Tricophyton gypseum*. Citron,[11] in experiments conducted with a view to producing an active or passive immunity against ringworm, treated rabbits with tricophyton cultures but was practically unsuccessful, although he was able to demonstrate the development of a moderate amount of precipitins.

Recently, Montpellier and Boutin [12] undertook to determine whether the favic organism reacted vis-à-vis with the mycotic infection, and, having tried vaccinotherapy (substance not noted), came to the conclusion that there is an absence of antibodies detectable by means of the complement-fixation test when using heated serum for the test and on their presence with nonheated serums.

THE ANTIGEN

Phytins (Favine, Tricophytin, etc.).—In 1902, Neisser [13] (posthumous work of Plato) described an extract of tricophyton cultures which he termed tricophytin. The original tricophytin was prepared from an organism obtained from a deep form of tricophytic folliculitis. It consisted of the filtrate of the organism, filtered through sterile filter paper after the organism had been grown at room temperature on 4 per cent. maltose bouillon for two months and then broken up as much as possible with a glass rod. Phenol was added to the filtrate as a preservative. Bloch and Massini [1] used Plato's phytin in their experiments, with the exception that they filtered the organism through Chamberland filters, thus absolutely excluding the passage of fungus particles or spores into the filtrate. Others grew their organisms on solid mediums for a variable period of time, ground it up with salt solution or salt crystals and then heated the suspensions to various temperatures for sterilization, thus in reality using fungus vaccines.

Neophytins (Neofavine, Neotricophytin, etc.).—The antigens used in these experiments are somewhat different from the phytins and vaccines used by Plato and his successors. They are a combination of the two types of antigens previously used. For the preparation of the neophytins, only fungi which were definitely pathogenic both in the human subject and the guinea-pig at the time of culture were selected. The organism was grown at room temperature in an Ehrlenmeyer flask containing 50 c.c. of 4 per cent. maltose bouillon. Neofavine (*Achorion*

11. Citron: Ztschr. f. Hyg. u. Infectionskrankh. **49**:120, 1905.

12. Montpellier and Boutin: Ann. de dermat. et syph. **8**:569, 1923.

13. Neisser: Plato's Versuche über die Herstellung und Verwendung von Tricophytin, Arch. f. dermat. u. syph. **40**:63, 1902.

quinckeanum) was grown for two months; neotricophytin (*Tricophyton gypseum*) was grown for six weeks; neomicrosporin (*Microsporon lanosum*) was grown for four weeks; neoepidermophytin (*Epidermophyton inguinale*) was grown for six weeks. In the final experiments, this last neophytin was not used owing to the rapid loss of pathogenic properties of that organism when grown artificially. The growth

Fig. 1.—Isolated favus of the back before neophytin injection. The large splotches are stains from tincture of iodin applied to lesions several hours before the photograph was taken. The limits of the lesions themselves are seen in the centers of these splotches.

and culture medium was then poured under aseptic precautions into sterile bottles containing glass beads, placed in a shaking machine for twenty-four or more hours or until the organism was so divided and broken up that the resultant suspension could pass easily through a 22 gage needle. It was then sterilized at a temperature of 68 C. for one hour, tested for sterility after 0.5 per cent. phenol (1 c.c. of a 5 per cent. solu-

tion for every 10 c.c. of suspension) had been added. Owing to the marked acidity of the suspension, it was neutralized by the addition of sterile 0.3 per cent. sodium bicarbonate solution in the portion of 1 : 10. This brought the reactions of the suspensions to figures varying from p_H 7.6 to p_H 8. Some of the experiments were conducted with non-neutralized and others with neutralized suspension.

SKIN REACTIONS OBSERVED WITH MALTOSE BOUILLON, RINGWORM VACCINE, PHYTIN AND NEOPHYTIN

Maltose Bouillon.—In normal children and adults, there is no reaction either locally or generally from the intracutaneous injection of 4 per cent. maltose bouillon up to 0.25 c.c. This is likewise the fact for subcutaneous injections in amounts up to 0.50 c.c. In syphilitic persons, these amounts given intracutaneously and subcutaneously, respectively, cause slight but definite papulation. In guinea-pigs, there is no local reaction in amounts up to 1 c.c. given subcutaneously. In young guinea-pigs, there may be slight papulation with the larger dose.

Simple Vaccine.—These were prepared in the same manner as ordinary vaccines by scraping off the fungus grown on a solid medium, but grinding it up with sodium chlorid crystals and then diluting with salt solution. Depending on the dilution, the reaction at the site of the injection, in human subjects, either intracutaneously or subcutaneously, is quite marked and in many instances pustular. This is true for dilutions up to No. 8 of McFarland's nephelometer in doses up to 0.25 c.c. by the intracutaneous route and up to 0.5 c.c. by the subcutaneous route. The reaction is likely to be most marked when injected intradermally. In guinea-pigs, it is usually pustular, likewise depending on the dosage and the dilution. It is certain that these reactions can be avoided only by a considerable dilution of the vaccine and the use of minute doses of these highly diluted suspensions. It is just as certain that the greater the dilution and the smaller the dosage, the less marked is likely to be the antigenic action. In the guinea-pig, three doses, at four day intervals, in 0.5 c.c. doses (dilution equivalent to No. 8 of the nephelometer) causes slight but definite shortening of ringworm infection with the organisms already noted.

Phytins.—Given in doses of 0.5 c.c. to 1 c.c., or even smaller doses, intracutaneously, subcutaneously or even rubbed into an abrasion, these may produce in persons who have had ringworm a local reaction. The reactions are most marked in patients suffering with ringworm infections. In these patients with ringworm, there occurs a local reaction in the form of an itching papule at the site of injection, a general reaction in the form of fever, malaise, headache, etc., and a focal reaction.[14]

14. Amberg, S.: J. Exper. Med. **12**:435, 1910.

According to Bloch and Massini,[1] a focal reaction occurs only in patients with acute or deep ringworm.

In guinea-pigs, whether normal or presenting ringworm infections, there is no reaction in doses up to 1 c.c.

Neophytins.—Undiluted, non-neutralized neophytin, intracutaneously and in doses as low as 0.1 c.c., causes in the normal guinea-pig papula-

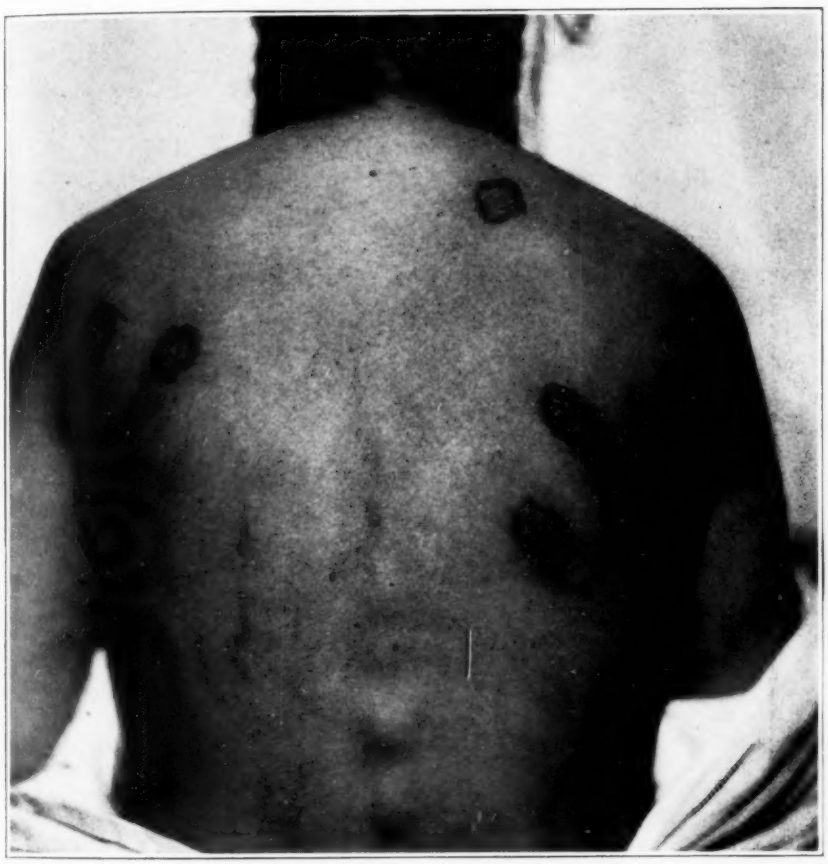

Fig. 2.—Focal reaction. This developed three days after intracutaneous injection of 0.25 c.c. of non-neutralized neophytin (neofavine). The lesions were almost twice as large as originally; all showed a well marked erythematous halo, visible around several of the lesions in the illustration. The halo disappeared in three days, although the lesions themselves appeared stationary with, however, eventual spontaneous cure. There was no general reaction. The local reaction was a papulopustule.

tion and pustulation and in the normal human subject, redness, papulation, and in most instances pustulation; when given subcutaneously and in the same dosage, the results are about the same. Injected into

guinea-pigs presenting ringworm inoculation "takes," the reactions are the same as in pigs that are free from ringworm infection. In the human subject, intracutaneous injections of neutralized neophytin (neofavine) in doses as high as 0.25 c.c. cause slight papulation. The same dosage of neutralized neofavine given intracutaneously three months after spontaneous cure of experimental favus in a human sub-

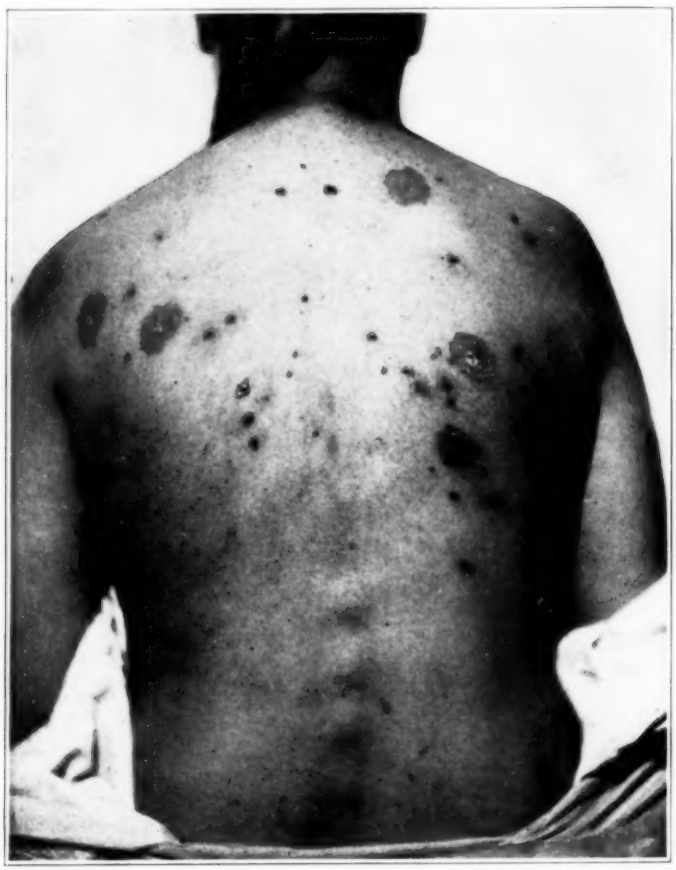

Fig. 3.—Multiple superinfection in isolated cutaneous favus which developed ten days after the intracutaneous injection of 0.25 c.c. of non-neutralized neofavine and at a time when the original (larger) lesions were undergoing spontaneous regression. They were not tricophytids as at first supposed; microscopic examination showed the crusts to be composed of fungus and the pure culture of *Achorion quinckeanum was obtained.*

ject (author) caused slight papulation and slight itching, but no reaction at the site of the healed lesion. On the other hand, if non-neutralized neofavine is given intracutaneously in the same dosage in isolated favus of the skin, there is produced a focal reaction (Figs. 1 and 2)—a local

pustular reaction, but apparently no general reaction. As already noted, the neophytins when diluted and neutralized give local reactions that are considerably modified as compared with those resulting from non-neutralized neophytins, but they are definite and sufficiently marked in the normal human patient. In one case of kerion celsi, the intracutaneous injection of 0.25 c.c. of non-neutralized neotricophytin appeared to be followed by a focal reaction in the form of an apparently more rapid healing of the lesion. Significant focal reactions did not appear to be present following the intracutaneous injection of non-neutralized neofavine, dosage 0.25 c.c., in two cases of superficial ringworm of the scalp.

In the guinea-pig, neutralized neophytins injected in a dose of 0.5 c.c. intracutaneously or subcutaneously produce papulation but no pustulation.

In a human subject with isolated cutaneous favus of the skin, the intracutaneous injection of non-neutralized neofavine, dosage 0.25 c.c., was followed by multiple superinfection, probably the result of a lowered skin resistance similar to that which occurs in the lungs and elsewhere following an overdose of tuberculin (Fig. 3).

EXPERIMENTAL

A group of guinea-pigs were given six 0.5 c.c. dermohypodermic injections each, at three day intervals, of non-neutralized and neutralized neophytins (neofavine, neotricophytin and neomicrosporin). Ten days after the last injection, they were inoculated, as were controls, with their respective organisms.

Favus inoculated and vaccinated guinea-pigs (non-neutralized neofavine) showed spontaneous cure in twelve days (control twenty-nine days); tricophytin inoculated and vaccinated guinea-pigs (non-neutralized neotricophytin) showed spontaneous cure in sixteen days (control twenty-four days); *Microsporon lanosum* inoculated and vaccinated guinea-pigs (non-neutralized neomicrosporin) showed spontaneous cure in twenty-seven days (control fifty-one days). The duration of the infections produced by the crossed immunity tests were about the same, and the immunity was at least three months in duration.

The pigs vaccinated with neutralized neophytins showed that they had developed some immunity, but to a far less marked degree than the pigs that received the non-neutralized neophytin injections.

COMMENT

Since the phytins produce no immunity in the guinea-pig (and these animals certainly develop a rapid spontaneous immunity) and no focal reaction in superficial ringworm infection in the human subject, there

is little reason to suppose that they produce any marked immunity in the human being. On the other hand, we have been able to shorten definitely the period required for spontaneous cure of ringworm in the guinea-pig by vaccination with the neophytins. Furthermore, we have been able to show that an immunity reaction, in the form of a focal reaction in a superficial type of ringworm (cutaneous favus), follows the intracutaneous injection of a small amount of neophytin.

Unfortunately, dead or living fungus protoplasm, when injected into the skin or subcutaneously, causes the development of pus in most instances in both the experimental animal and the human subject. Under such circumstances, it follows that, although we definitely know that the neophytins possess the proper antigenic properties for the induction of a ringworm immunity, they cannot, unmodified, be used for therapeutic purposes in ringworm infections. In a way, the local reaction after a neophytin injection may be compared to the production of a "fixation abscess." There are few instances in ringworm infections in which the production of multiple "fixation abscesses," with immunization in view, appears justifiable.

SUMMARY

1. In superficial ringworm infections of guinea-pigs and human beings, the injection of phytins (culture filtrates of fungi) produces no focal reactions indicative of antibody production.

2. In one form of superficial ringworm infection in the human being, the injection of neophytin produced a focal reaction indicating the presence of some degree of antibody production.

3. In guinea-pigs, six injections of non-neutralized neophytin, in doses of 0.5 c.c. each, shortened the duration of the experimental infection and hastened the degree of spontaneous recovery.

4. In their present unmodified state, the neophytins cannot be used in human beings, with prophylaxis or therapeusis in view.

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TREATMENT OF COMMON WARTS BY NEO-ARSPHENAMIN

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Little is know about the causation of the various types of warts, including the ordinary verruca vulgaris. That the latter is infectious seems quite probable. Authors discussing the treatment of common

Fig. 1.—The condition in this case had been growing worse for a year, before seen by the author, under treatment with mercuric chlorid.

warts, place little emphasis on the use of arsenic, although it is mentioned in all textbooks on dermatology. Many patients suffering from diseases of the skin with a verrucous element are benefited by the

administration of arsenic. I believe there are many cases in which the intravenous injection of neo-arsphenamin is justifiable in the hope of accomplishing, by intensive arsenical treatment, what may not be possible with milder forms of arsenic.

A patient with multiple warts of the scalp was recently treated unsuccessfully by me with various therapeutic methods, including the roentgen ray, fulguration and mercury (the latter both externally and

Fig. 2.—Two months after injections of neo-arsphenamin. This shows the remarkable regrowth of hair after the disappearance of the warts.

internally). The largest lesions had been removed, but new lesions continued to appear. After unsuccessful administration of solution of potassium arsenite (Fowler's solution), I tried heroic doses of sodium cacodylate, but with no result. As a last resort, my patient was given an intravenous injection of 0.6 gm. of neo-arsphenamin. At the end of a week, the lesions had all disappeared, although there was a slight recurrence at the end of three weeks. A second similar injection was then given and was followed by permanent recovery.

THE ITCH MITE AND ITS BURROW

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The history of scabies dates far back. Rabelais says that Anak was expert in eliminiting the itch mite from the fingers.[1] Anak lived before the time of Moses, and his children, the Anakin, were giants so large that ordinary people looked to them like grasshoppers. This superior attitude is not unusual, but it seems that the converse was also true, that the rest of the community regarded themselves, in contrast with the children of Anak, as grasshoppers, a surprising exhibition of humility.[2] Rabelais does not mention whether Anak restricted his medical attentions to his own family, but under the circumstances it is altogether probable that he did so.

Many persons nowadays do not take Rabelais seriously, and even I at times feel toward him like the Irish bishop who, on reading "Gulliver's Travels," laid down the volume with the remark that he did not believe that half the things related in that book were true.

Turning to more recent medical discoveries, Riehl[3] says that Avicenna (980-1037) recognized scabies as an independent disease, and knew the cause of the affection.

For ages, scabies was considered a constitutional disease. Dr. C. G. Cumston,[4] in an excellent article recently published, relates that the first modern demonstration of the itch mite was made by Dr. J. C. Bonoma of Leghorn, Italy, in 1687.

It is also related that he learned this procedure from the galley slaves in the harbor, who used to pick out the itch mites from their burrows in the skin of their comrades. The acarus was first demonstrated before a medical class in Alibert's clinic in Paris, in 1834, by a young Corsican named Ranucci, who had learned it from the peasant women in his native island. In both instances, the discoverer was an Italian who had learned the method from the common people. Possibly this circumstance was not altogether accidental. In the case of the galley slaves, they were boys with good sharp young eyes, and in the case of the peasant women they were probably girls with equally sharp organs of sight.

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1. Pantagruel, Chapter 1.
2. Book of Numbers, XIII, p. 33.
3. Riehl, G.: Allgemeine Dermatologie, Lehrbuch d. Haut u. Geschlechtskrankheiten, E. Rieke, 1914.
4. Cumston, C. G.: Brit. J. Dermat. & Syph., January, 1924.

I have a great deal of consideration for those who clung to the old belief that scabies was a constitutional disease. In the first place, they were trained to do so, and furthermore, even nowadays, one often has difficulty in differentiating between eruptions due to internal causes and those arising from the itch mite. Modern cleanliness and the frequent use of chemicals often so mitigate the eruption, and so blot out evidence, that the finding of conclusive facts is frequently most difficult. There are, however, few diseases that are less constitutional than scabies. If a person sleeps with an infected individual, or in a bed recently occupied by an infected person, he almost inevitably contracts the disease. It is almost never acquired in any other manner, and so is often called a venereal disease. This cubicular mode of transmission is due to the mite being a night wanderer, a noctambule.

THE BURROW OF THE ITCH MITE

Both the male and the female feed on the rich juices of the rete malpighii. The male makes a shallow hole, just deep enough to obtain the juice necessary for himself, but the female has not alone to feed for herself but also for her progenital work, and her embryos also must have nourishment for a short time. She, therefore, bores a long burrow, well beneath the horny layer, and finally dies at the end of her burrow. On the surface this burrow is indicated by a roughened, white line, not straight, but having one or two obtusely angular deviations. These deviations are only such as any burrowing animal makes, as every boy who has ever tunneled in a haystack knows. The roughened white line may become black by the deposition of dirt in the roughened epithelium. The burrow is usually not more than a quarter inch (0.6 cm.) long, but I ran across one once that was a full inch (2.5 cm.) in length. It was so long and so rough that I at first thought it an ordinary scratch. The little pustule at its distal extremity was, however, very characteristic. In slicing it off, in a manner presently to be described, it was seen to be a burrow with masses of feces scattered along its course. No eggs were found, as these had evidently hatched out, and the embryos had escaped to the surface.

THE VESICLE ATTENDANT ON THE BURROW

At one end of this white line a minute clear vesicle, later turning into a pustule, may be found, indicating the situation of the head of the female mite, and if one wishes to emulate the example of Anak, one may push a needle under the vesicle in the direction of the burrow, and so succeed in bringing up the female on its point, as a minute white ball, looking to the naked eye like a tiny milium ball. Such a demonstration requires considerable dexterity, and even then the fishing is uncertain, and furthermore unnecessary.

The evident reason for the appearance of the vesicle is the disturbance caused by the insect in eating her way forward in the tunnel. It may even be that she secretes a dissolving saliva, which is serotoxic. To us, however, the vesicle serves a much more important purpose than to indicate the situation of the head of the insect. Whenever vesicles appear on the sides of the fingers, they may be due to scabies or to

The elbow tip in a patient suffering from scabies. The papules were so large and rough as to simulate those of lichen hypertrophicus.

the epidermophyton; or possibly to salol, phenol or iodoform—many cases of dyshidrosis have been of this origin. A correct diagnosis, therefore, makes all the difference between concluding whether one has to deal with a most refractory condition or one quickly curable.

LOCATIONS IN WHICH BURROWS MAY BE FOUND

Like every parasite, the itch mite has its favorite locations, which are between the fingers, around the wrists, over the elbow tips, on the

axillary folds, especially the anterior one, in the gluteal folds, and in the female on the nipples, in the male both on the shaft and on the glans penis, and in the infant on the feet, especially in the instep. Although these are the classic situations for the eruption, they are not all equally favorable for finding the burrows. The best places are between the fingers and on the front of the wrist, and the neighboring palm, especially along its ulnar border. The glans penis is also a good situation on which to find the burrows. It is difficult to see them on the rough skin over the elbow tips and on the rugous nipple; and even when seen in these localities, it is difficult to be sure of them. Rarely one may find a burrow on the anterior fold of the axilla, but when they are present in the hollow of the foot they may be well outlined. As for the rest of the cutaneous surface, the hunt is like searching for a needle in a haystack.

As may be inferred from the foregoing, the hands and the wrists are the most favorable situations for this kind of hunting, but in private practice this may completely fail. As indicated before, constant scrubbing of the hands, and the frequent use of antiseptic toilet articles may keep this locality free and obliterate all evidence. At the other extremity of the scale are those cases in which the eruption is so abundant as to hide the burrows.

The following is an interesting instance showing the difficulties attendant on a demonstration. The patient was a boy, over 5 years of age, with a widely distributed, itchy, papular eruption. Even the cheeks were rough and blotchily reddened, which would seem to exclude scabies. A granular appearance of the eruption on the skin of the abdomen, and some raised, red, dry, ten cent piece sized, circular patches on the outer surface of the left thigh caused me to be suspicious. This caused me to look between the fingers, where there were some insignificant lesions; at the penis, where there were two light red, indefinite spots; then at the scrotum, where there was one spot a little redder and more thickened. Finally, the feet were examined, and burrows were found.

DEMONSTRATION OF THE BURROW

I have spoken of the demonstration of the itch mite by fishing for it with a needle. A better way is to pinch up a fold of the skin with the burrow running along the summit of the fold, and with a scalpel shave off a slice of epidermis containing the burrow, and then to lay the slice, bottom side up, in glycerin on a glass slide, and place over it a cover glass and examine with a low power lens. If fortunate, and you almost always are, you will include a portion of the burrow containing possibly an itch mite, but almost assuredly eggs and feces, which are equally conclusive evidence, as they are plainly visible and totally unlike anything else found in the skin.

One might well ask why so much effort should be made to find the itch mite and its burrow in such a well defined disease as scabies which, when well developed, any layman can recognize. Unfortunately for this view, there intervenes the well-known principle of the nonspecificity of symptoms. The response of any animal or organism to similar stimuli is not always precisely the same. As Bayliss has remarked, there is no fatal necessity about any such reactions, and it is the reactions that constitute the symptoms. The following cases will illustrate what I mean.

A man consulted me, Aug. 24, 1917, with a well marked, large papule on the cutaneous surface of the foreskin. The rest of the eruption was distributed in the classical situations. The itching at night was characteristically intense, and one egg was found in a burrow. His wife also had an itchy eruption of the skin, but here entered the peculiarity of the case. We could find no burrows, and no trouble on the nipples or between the fingers, but there was a great deal of cutaneous irritation all over the trunk, arms, forearms and thighs, and there was a papular eruption under the breast. The itching was severe at night. She had a papular eruption with scratch marks across the shoulders. This is supposed by some to be pathognomonic of phthiriasis, but it is not, as it may occur, although seldom, in other affections. In other words, if she had consulted us alone and we had not known of her husband's case, I am sure we should have failed to make a diagnosis.

COMMENT

I have given a few of the details of this most interesting disease, but by no means all of them. Voltaire once said that all writing is good provided it is not tiresome, and he did not leave one in the dark regarding what he considered tiresome. He said, "If you wish to be tiresome, say it all."

A CHRONIC ITCHING PAPULAR ERUPTION OF THE AXILLAE AND PUBES (FOX AND FORDYCE)

REPORT OF TWO CASES

FRANK CROZER KNOWLES, M.D.
AND
PATRICIA HART-DRANT, M.D.
PHILADELPHIA

The first case of this unusual condition was reported by Fox and Fordyce in 1902. The eruption was of a papular character, and the lesions were numerous, small, firm, smooth and rounded. The skin was deeply infiltrated and slightly fissured. The aggregated papules were of normal color or but slightly reddened, although the scratching produced at times a considerable amount of congestion and excoriation. The disease involved the axillae chiefly, and in a lesser degree the pubic region was involved. Fox recorded another case of a similar character in this same communication.

Since the original description of this condition, cases have been reported by Fordyce, Haase, Rasch and Kissmayer, Brocq, Burnier and Bloch, Withers, Beatty, Walter, Barber, Adamson and Whitfield. Twenty cases have been recorded including the two in the present paper. All, with the exception of one recorded by Fox, have occurred in the female sex. Most of these cases have been observed in neurotic, highly strung women, some being in rather poor health and anemic. The youngest patient in the cases recorded was a girl aged 13 years.

Pruritus has been a marked feature, the itching in most of the cases interfering with sleep, undermining the health still further, and has been mainly uninfluenced by the many applications employed, including the roentgen rays.

The disease has been limited to the axillae, the axillae and pubic region, and in a lesser number an outbreak has been observed around the nipples, and occasionally on the lower abdomen.

The eruption in the reported cases conforms closely to the original description of Fox. Two cases of this disease have been observed.

REPORT OF CASES

CASE 1.—Mrs. E. D. M., white, a girl, aged 17, entered the Woman's Hospital, Jan. 5, 1922, complaining of intense itching in the axillae and over the pubic region. The condition appeared first in the right axillae in October, 1922, as a severe itching and burning. In a few days, an eruption was noticed which resembled prickly heat and which soon took the form of the papular lesions. On December 1, the left axilla became affected in the same manner as the right, and

two weeks later a few papules appeared on the pubis. The patient was a large well nourished young woman, whose health had always been good. Her past medical history was negative. She had had all the diseases of childhood, and influenza in 1918. The family history was negative. Menses began at 11 years of age and had since been normal.

The patient said she was "very nervous" and was taking medicine prescribed by her family physician for her nerves. She was troubled with insomnia and had severe paroxysms of itching during the night.

Fig. 1 (Case 1).—Pruritic eruption in axilla.

The papules were uniform, smooth, shiny, hemispherical and translucent, with a slightly pinkish cast at the base and at each follicle. They were deep-seated and firm. The intervening skin was slightly but not definitely pigmented, and there was no induration. The papules had a moniliform arrangement following the finer lines or lines of cleavage of the skin. The older lesions were slightly umbilicated, and in some of the papules a tiny black plug appeared at the apex of the dome, while a few seemed to be capped by a delicate scale. The patient never had had a growth of hair in the axillae and the pubic hairs were scant and lusterless, having been present about one year.

On examination of the axillae with the binocular binobjected microscope, considerable variation was found in the form of papules. The smallest ones

were domelike and appeared to contain a milky material. The surface was slightly scaly. The slightly larger ones showed a flattening or umbilication. In one or two instances, short hairs extended upward from the center; in these and also in some of the rounder ones, shorter or longer hairs projected. No additional features were found in the deeper parts of the skin after cleansing with paraffin oil and applying a cover slip. The liquid petrolatum did have the effect of making the lanugo hairs more visible on strong illumination.

The patient perspired little during the examination. She had never used a depilatory or a deodorant. The itching was most intense and of a paroxysmal character.

Laboratory Findings.—The blood Wassermann reaction was negative; the urine was normal; blood examination revealed 5,460,000 red blood cells, 5,800

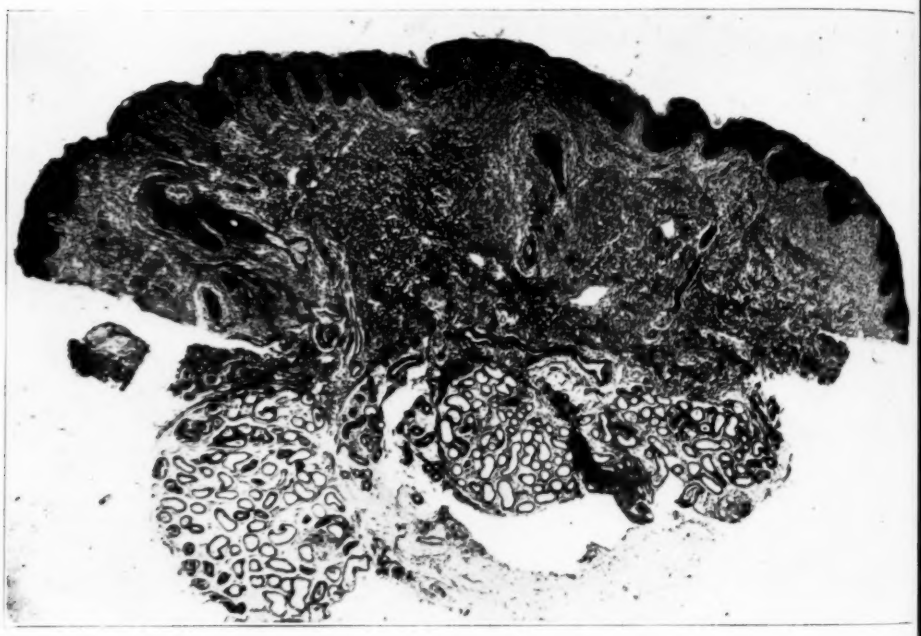

Fig. 2 (Case 1).—Location of growth. Most prominent feature is dilatation of sweat gland coils.

white blood cells, and 65 per cent. hemoglobin. Differential count revealed: 55 per cent. polymorphonuclears; 30 per cent. small lymphocytes; 11 per cent. large lymphocytes, and 4 per cent. eosinophils.

Anaerobic and aerobic cultures made from the lesions were negative except for *Staphylococcus albus.*

A roentgenogram of the sella turcica showed no roentgenographic evidence of erosions. The capacity of the sella turcica appeared to be within the usual limits.

Treatment and Course.—Treatment consisted of antipruritic and keratolytic agents either in the form of salves or lotions, and did not control the subjective symptoms or alter the appearance of the lesions. The patient was given three roentgen-ray treatments, which did not relieve the condition, and she refused further treatment.

When the patient was last heard from (Dec. 17, 1923) she said the lesions had not changed in character, although she had been at the seashore most of the summer. She had had about two paroxysms of itching daily, but they did not annoy her as much as at the onset, and her nervous condition was much improved.

Case 2.—A woman, aged 28, colored, married, a housewife, born in Philadelphia, whose family history and whose past medical history were negative except for measles during childhood and influenza during the pandemic of 1918, from which she had made a good recovery, had had no cough and no loss of weight. Her appetite was good and her bowels moved regularly

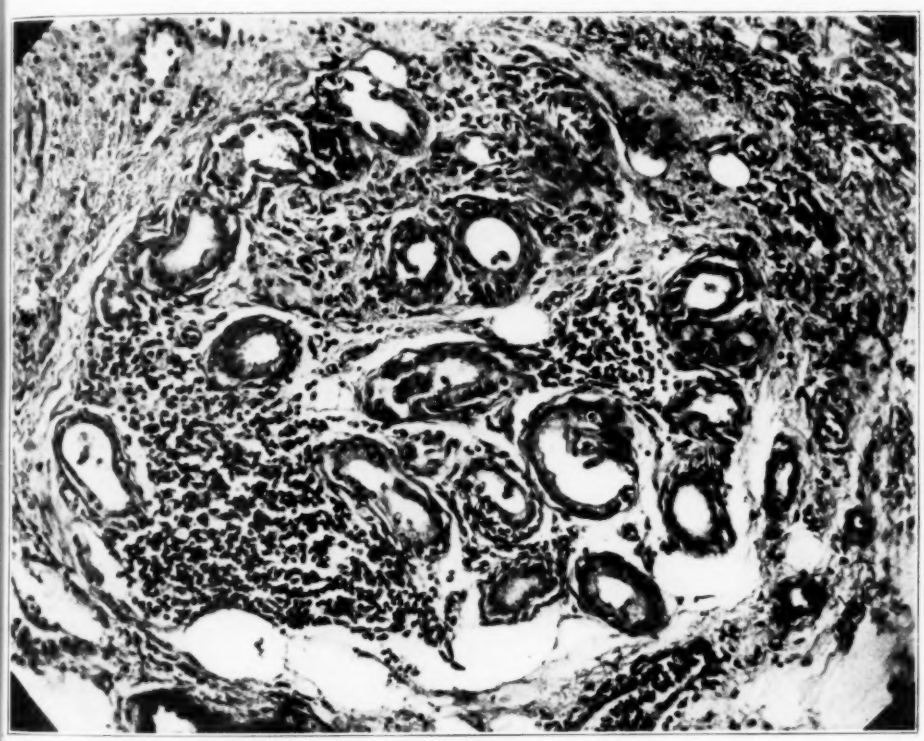

Fig. 3 (Case 1).—High power magnification shows cellular infiltration, dilatation of sweat gland coils and degeneration of their walls.

without laxatives. Menses began at 14 years of age; the periods were regular from the beginning, at twenty-eight day intervals, and lasting three days. She had no dysmenorrhea. There had been no pregnancies.

During 1921, she contracted syphilis. During June, 1922, the patient applied a patent deodorant to her axillary region. During July, she had noticed pruritus in this region. The pruritus became worse, and she shaved her axillary hair. The hair did not grow again. At this time, she noticed a papular eruption, and the pruritus became progressively more intense. This papular outbreak conformed in all details to that in Case 1. The same papular outbreak was present in the pubic region. During October, 1922, she sought treatment for

syphilis and was referred to the outpatient skin department of the Pennsylvania Hospital by Dr. Bayard Stewart. Intensive antisyphilitic treatment was given. The Wassermann test had remained negative for the last nine months. This curious outbreak had been unaffected by the arsphenamin and mercury injections. All of our efforts with local applications, including the roentgen rays, were without avail.

HISTOPATHOLOGY

Case 1.—Three blocks of tissue were made. The parts which are adjacent to the hair follicle orifices were somewhat acanthotic. There was a cellular infiltration, especially around the hair follicles and the blood vessels and to a lesser degree between the coils of the sweat glands. This infiltration consisted chiefly of lymphocytes distributed on a very fine reticulum; in other portions of the sections, however, spindle cells predominated. The tissue interstices in such places were widely distended by fluid.

The cells of the hair follicles were apparently hyperplastic, and the lumina were broadened and crowded with keratinous detritus. Lanugo hairs were often found within them. Polymorphonuclear leukocytes predominated in many of the blood vessels, in both the capillaries and the arterioles.

The sweat glands in the deepest part of the section showed widely distended coils, and the presence of foci of closely packed lymphocytes indicated an inflammatory process.

In no part of the numerous sections examined could definite cystic accumulations, either of fluid or of keratinous material, be discovered. Giemsa preparations did not reveal bacteria.

Case 2.—A moderate hyperkeratosis was present. The hyperkeratotic epidermis extended into the follicles and plugged them. Acanthosis was a marked feature; also an intracellular and extracellular edema in the prickle cell layer. Atrophy of the lining cells of the convoluted portion of the sweat glands with marked dilatation was characteristically exhibited. A perivascular round cell infiltration was also observed.

LITERATURE ON THE SUBJECT

Fordyce [1] made the histologic investigation in Fox's original case, and recorded: (1) a hyperkeratosis involving chiefly the sweat-duct orifices, their intra-epidermic portions, and the orifices of the hair follicles; (2) consecutive hypertrophy of the stratum spinosum (acanthosis) surrounding the altered sweat ducts and hair follicles; (3) mechanical dilatation of the coil glands, which resulted in changes in their epithelial lining; (4) inflammatory changes of a more or less chronic character in the derma.

Fordyce,[2] in a subsequent paper in 1909, reported an acanthosis, most marked about the sweat duct, and a hyperkeratosis in the form of a plug filling the mouth of the duct. Intracellular and extracellular edema was present, and contiguous to the duct minute vesicles had formed. In the corium, the striking feature was the dilatation of the sweat coils. Some of the tubules contained partial or complete casts,

1. Fox and Fordyce: J. Cutan. & Genito.-Urin. Dis. **20**:1, 1902.
2. Fordyce: J. Cutan. & Genito.-Urin. Dis. **26**:187, 1909.

and the lining cells had undergone a parenchymatous degeneration. An infiltration of lymphocytes and plasma cells sheathed the vessels and was aggregated about the coil. There was also a proliferation of fibroblasts. The capillaries were dilated and filled with blood. In places the collagenous tissue of the corium had undergone a mucoid degeneration.

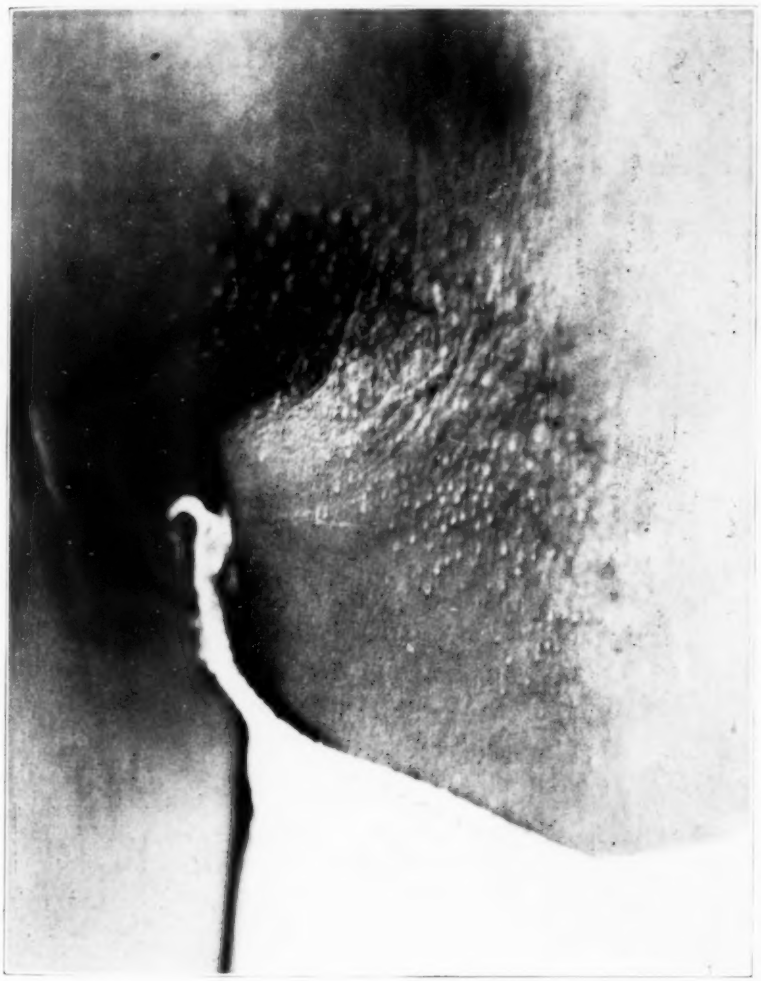

Fig. 4 (Case 2).—Eruption on arm.

Haase's[3] description differed only slightly from Fordyce's in the added features of hyaline degeneration of the arteries and the change

3. Haase: A Chronic Itching Papular Eruption of the Axilla, Pubes and Breast, J. A. M. A. **56**:174 (Jan. 21) 1911.

in the staining quality of the elastic fibers. The most marked changes found by Haase was the dilatation of the sweat glands, accompanied by a degeneration of the lining cells. In some of the tubules, there were partial casts, and in two were round concretions or bodies, the nature of which was obscure to Haase.

Walter recorded an acanthosis without parakeratosis, but there were large, irregular pale cells at both the sweat glands and the hair follicles.

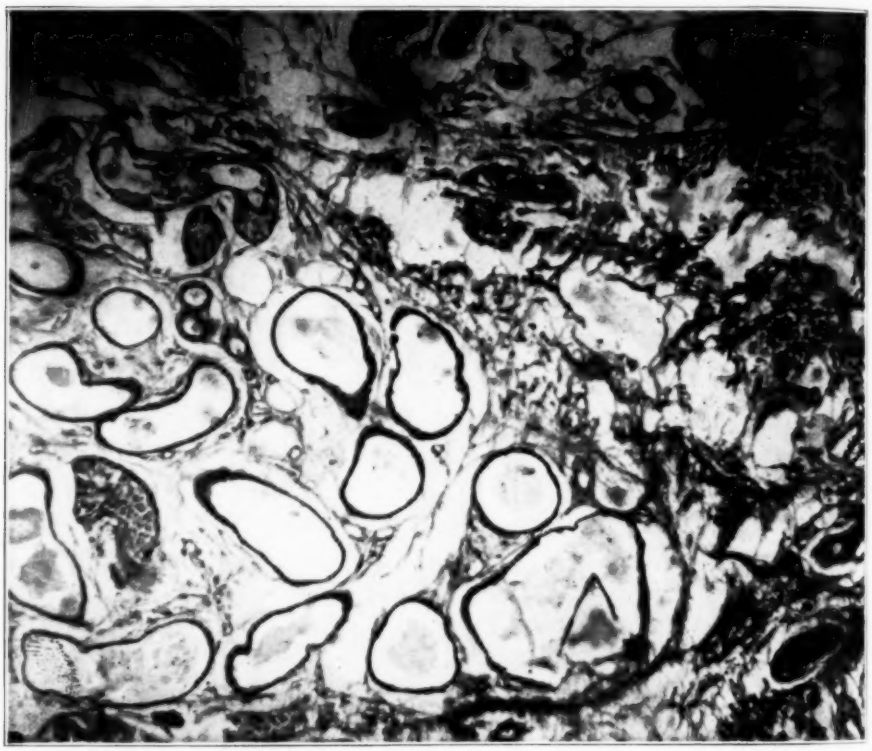

Fig. 5 (Case 2).—High power magnification, shows marked dilatation of sweat gland coils and marked degeneration, almost complete, in some of the walls.

Whitfield [4] found little or no hyperkeratosis, but marked acanthosis, forming a small succulent warty growth, extending both upward and downward into the true skin. The growth was formed around the intra-epidermic portion of the sweat canal as a center, the canal being more acutely curved than is normal. Below in the true skin there was a hemispherical fibroblastic infiltration with the formation of new col-

4. Whitfield: Brit. J. Dermat. **35**:393, 1923.

lagenous tissue, apparently an attempt to circumscribe the down growth of the epithelium.

Withers mentioned that he found the most striking change in his section in the enormous dilatation of the deep convolutions of the sweat gland and the hyaline degeneration of the lining. He found that the pathologic changes in brief consisted of an acanthosis with hyperkeratosis, edema, perivascular infiltration and changes in the sweat glands, with keratocystomas of the sweat glands.

There is a considerable diversity of opinion as to the etiology of the condition. According to Fordyce, the histologic changes as found in the first case of this condition resembled markedly those seen in porokeratosis, except the sweat gland changes. Clinically, however, there is not the slightest resemblance.

Fordyce, in a later communication, referred to the relationship of this condition to neurodermatitis, advancing the hypothesis that some toxic substance in process of elimination is responsible for the changes. Repeated traumatism of the epidermic cells, as from scratching, produced the acanthosis and hyperkeratosis. He believes that there is justification in calling this condition a variety of neurodermatitis, probably toxic in origin.

Haase "suggests that the pathological condition began in the sweat glands, with a morbid change in the lining cells and a dilatation of the gland proper, and that all other changes demonstrated were secondary to this process, and due to the elimination of a toxin yet unknown."

Withers [5] believes that this is a chronic circumscribed dermatitis of neurogenic origin.

Darier, in discussing a case of this character, stated that the lesions did not resemble those seen in the lichen simplex of Vidal.

Adamson pointed out the close similarity of the lesions to plane warts.

Barber suggested that the lesions were due to chemically altered and irritated sweat.

Colcott Fox, in abstracting Fordyce's second paper, recognized that the disease was not ordinary lichenification but an independent and well defined clinical entity and not due to mere friction of itching skin.

Whitfield agrees with Adamson that the little papules resemble plane warts clinically and microscopically, except that much of the new growth takes place downward into the true skin.

Whitfield suggests that the condition is dependent on a disorder of the suprarenal sympathetic system. The points on which he bases this conclusion are the neuresthenia, the loss of muscular tone and the

5. Withers, S. M.: Chronic Papular Itching Eruption of Axillae and Pubes, Arch. Dermat. & Syph. **1**:8 (Jan.) 1920.

abnormal low blood pressure. He emphasizes the resemblance, notwithstanding the marked differences, to acanthosis nigricans.

Whitfield believes the term "acanthosis circumporalis pruriens" is more descriptive than the present title.

COMMENT

There are certain distinct and characteristic features in the present disease: 1. All the cases, with one exception, have occurred in the female sex, mostly those of a markedly neurasthenic type. The areas of involvement have largely been the axillae and pubic region, in which sweat secretion is normally marked. 3. The most characteristic histopathologic change has been dilatation of the sweat ducts and degeneration of their walls.

Two theories of causation that have been suggested are: (1) that it is a variety of neurodermatitis (Fordyce), and (2) that it is an atypical form of acanthosis nigricans (Whitfield).

In Brocq's "neurodermite chronique circonscrite" there was a marked acanthosis and some parakeratosis. The papillae were hypertrophied in all directions and edematous at their lips. A lymphocytic infiltration was present about the vessels and pilosebaceous apparatus. The sudoriferous glands were healthy.

In Brocq's neurodermatitis, the outbreak is not limited to the areas attacked in the present cases; in fact, is more often found elsewhere. Histologically, the picture in these cases is very much the same as in the disease described by Brocq, with the notable exception that the most characteristic feature found in our cases, dilatation of the sweat gland ducts and degeneration of the walls, is absent in neurodermatitis.

Acanthosis nigricans offers such a clear and distinct picture, with the presence of abdominal malignant disease, the marked pigmentation and the mucous membrane involvement, that the presence of an acanthosis seems to be the only point of resemblance between this disease and the one under discussion.

This disease therefore is apparently a separate entity, and a suggestion as to causation seems to be that some derangement of the endocrine system has caused an alteration in the sweat secretion, with a dilatation of the sweat ducts and degeneration of their walls, in the axillae, pubic region and occasionally elsewhere, and the irritation from altered sweat has secondarily caused an acanthosis and hyperkeratosis.

FAMILIAL STUDY OF THREE UNUSUAL CASES OF CONGENITAL ICHTHYOSIFORM ERYTHRODERMA*

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During the past three years, I have had under observation three cases of postnatal exfoliation which presented at the outset and during their subsequent development so much variance with any known clinical entity that until recently I have been unable to classify them. When seen early, the cases so closely approximated the picture of Ritter's disease (exfoliative dermatitis of the new-born) that for several months this diagnosis seemed acceptable. The fatal outcome of one case and the subsequent study of the remaining two led to a later diagnosis of an unusual form of the dystrophic type of epidermolysis bullosa. It is only within a few weeks, owing to the development of isolated ichthyosiform patches, that I have been able to satisfy myself that the cases are unusual variants of congenital ichthyosiform erythroderma.

The group of cases in question is deserving of report, moreover, by reason of the extraordinary family history and because of the suggestive factor of consanguineous marriage in the anamnesis. As may be seen from Figure 1, there are four children in the affected families, in whom only one, the oldest, a girl, has escaped. The remaining three male children are all affected in an identical manner. The parents of the affected children are two brothers who have married two sisters. The consanguineous factor is brought out in the fact that the parents are first cousins and the maternal grandparents of the patients are cousins twice removed. Of the affected children, the oldest is living at the age of 4 years.

The clinical description of any one of the three would fit the other two. The children are all undersized and somewhat marasmic. Scattered over the entire body and without any marked predilection, except that in all three the face and head are universally involved, is a remarkable form of superficial exfoliation. In all of the affected areas, this takes the form of thin sheets of epidermis, which apparently raise from an unreddened base and peel off spontaneously, precisely as

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* Studies and contributions of the Department of Dermatology and Syphilology of the University of Michigan Medical School, service of Dr. Udo J. Wile.

is the case in the exfoliative period of a scarlet fever. The amount of exfoliated epidermis in a day is enormous. The mere undressing of the children results in a veritable shower of larger and smaller flakes, and the proliferative process is so great that the clinical picture is in no ways changed by the incessant shedding. The most remarkable feature, however, lies in the fact that, as may be seen in Figures 2, 3 and 4, the desquamation occurs more or less irregularly, and there are relatively large areas of intervening skin, which, from the outset, have been unaffected. A careful, almost weekly, examination of the oldest child over a period of almost three years substantiates the fact that at no time have the unaffected areas, notably those on the back and buttocks

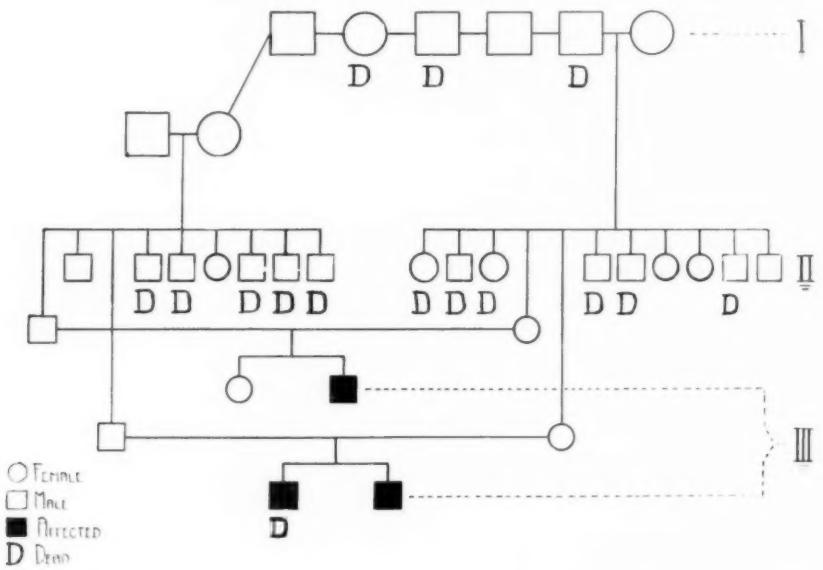

Fig. 1.—Family tree showing consanguineous ancestry as well as sex limitation in three cases of ichthyosiform erythroderma.

and scattered here and there on the abdomen, ever taken part in the exfoliative process. A similar degree of freedom of isolated areas of the body has also been noted in the remaining two cases. Except for the shins and over the knees, the exfoliation is of a thin type, represented by a few layers of the stratum corneum and until recently in no way resembling that seen in true ichthyosis or congenital ichthyosiform erythroderma. If a portion of the exfoliating skin be grasped by the fingers or the forceps, it can be peeled off for a considerable length, and apparently stops or breaks off at the margin of a healthy patch of skin. The color of the underlying skin for the first few moments is normal; very soon, however, it becomes reddened, remains so for a few

hours, is then restored to the normal color of the skin and almost immediately exfoliates again, repeating this cycle indefinitely. At no time have epithelial casts been noted.

Pruritus existed in the three cases, apparently was particularly distressing at night, causing loss of sleep, and was no doubt a contributory factor to the under-development and relative marasmus. This marasmus was extreme in the second case, and resulted fatally at the age of 11

Fig. 2.—Front view of first child.

weeks. Except for being undersized and underweight, however, there was nothing strikingly abnormal that could be made out in the clinical or laboratory examination in the affected children. A slight degree of polyadenitis, which might be expected, occurred in all. The blood picture was normal, the Wassermann reaction negative, and as far as could be made out, there were no evidences of persistent thymus or any other endocrine dysfunction.

Treatment, both local in the form of mild keratolytics, bathing and soothing applications in no way influenced the progress of the disease, nor was general treatment, in the form of arsenic, the cautious administration of thyroid extract, cod liver oil and iron, of any avail.

As stated in the foregoing, the diagnosis of Ritter's disease was first considered. The occurrence of two cases in families living together, the children having been born within a few days of each other, and

Fig. 3.—Back view of first child.

the striking clinical resemblance to this disease, made this diagnosis seem most likely. The children, moreover, were in actual contact, which lent color to the possibility of an infectious agent being responsible for the condition. The early death in one case, the persistence and metamorphosis of the disease in the other, naturally led to the abandonment of this diagnosis. The occurrence, two and one-half years

after the birth of the first child, of the third case with the same condition, made it certain that one was dealing with an epithelial cutaneous dystrophy, rather than with an infectious disease.

Although bullae have at no time been noted in any of the cases, the histologic picture of the disease was strikingly similar to that found in epidermolysis bullosa, notably as will be shown below in the histologic disorganization of the elastic tissue of the upper layers of the corium.

Congenital ichthyosiform erythroderma was first described by Brocq [1] in 1902, since which time a considerable number of cases have been reported from various parts of the world. These have all been

Fig. 4.—Youngest affected child.

collected and the subject has been admirably reviewed and presented by a monograph by MacKee and Rosen [2] in 1917.

According to their description, the disease is complex in its manifestations, and presents itself clinically and histologically in many diverse forms. The degree of ichthyosis may be slight or marked, although in general it is characterized by a pure hyperkeratosis. It

1. Brocq: Ann. de dermat. et syph. **3**:1, 1902.

2. MacKee and Rosen: Erythrodermie Congenitale Ichthyosiforme, J. Cutan. Dis. **35**:235, 343 and 511, 1917.

may be universal or scattered, erythematous, devoid of color or so markedly associated with pigmentation as to resemble acanthosis nigricans. Increase in the growth of the hair and nail is said to be an occasional finding.

Of extreme interest in connection with the histologic similarity of the group herein described to epidermolysis bullosa is the fact that MacKee and Rosen mention the occurrence of bullae and Nikolsky's sign in at least one case of congenital ichthyosiform erythroderma.

For the purpose of histologic study in the group described, biopsies were taken from the back and abdominal wall of the first and third

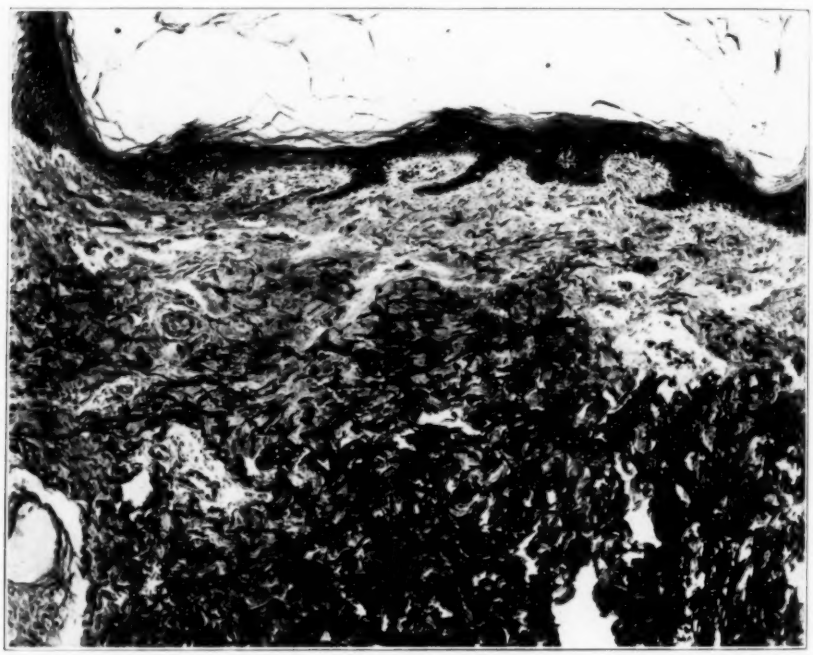

Fig. 5.—Engman's case of epidermolysis bullosa showing deficiency, fragmentation and disorganization of the elastica of the subpapillary layer (Weigert's stain).

affected children. The second child, as is noted in the foregoing, died at the age of 11 weeks, and a biopsy was not obtained from it. There can be no question that the changes described below for the two would fit the third. For purposes of comparison, the normal skin from the abdominal wall of the children of the same age was studied simultaneously. Through the kindness of Drs. Engman, Wise and Rosen, sections of the epidermolysis bullosa and congenital ichthyosiform erythroderma were also used in the comparative study of the anatomy of the cases herein described (Figs. 5 and 6).

The tissue was hardened in formaldehyd, cut in paraffin and was stained with hematoxylin, polychrome methylene blue, acid orcein, neutral orcein and Weigert's stain for elastic tissue.

HISTOLOGIC CHANGES

The Epidermis.—The main changes in the epidermis were those of an extraordinary acanthosis. The stratum corneum was conspicuous in all of the sections by its extreme thinness or absence (Figure 7). Herein lies a striking difference between these cases and the others described and all others of congenital ichthyosiform erythroderma, in which it has been stated that hyperkeratosis is the essential feature.

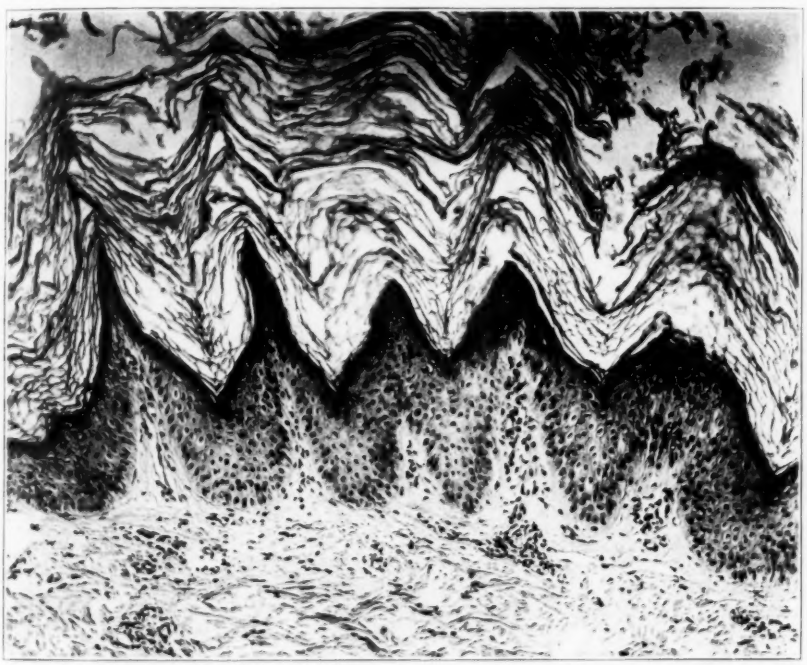

Fig. 6.—Section from typical case of congenital ichthyosiform erythroderma (MacKee and Rosen's case).

A few scattered areas of parakeratotic epithelium were seen here and there over the acanthotic rete (Figure 7). The most marked epithelial change consisted in enormous elongation and thickening of the rete pegs, marked thickening of the entire malpighian layer and an extraordinary degree of activity of the stratum germinativum.

The Cutis.—The main changes in the cutis were limited to the upper layer. Here a considerable degree of dilatation of the lymph spaces and capillaries and a slight leukocytic infiltration could be noted. The

most striking change, however, was that described by Engman and Mook for epidermolysis bullosa, in a marked diminution, disorganization and in places absence of the normal elastica of this layer (Figure 9). The collagenous fibers in the deeper layers of the cutis seemed to be well preserved, and no striking abnormality of the deeper layers of the cutis existed. The hair follicles, sweat ducts and sebaceous glands were all present and apparently normal.

To sum up briefly, the histologic changes in our group of cases consist in marked acanthosis with striking activity of the stratum germinativum, edema and disorganization of the elastica in the upper layers of the corium, analogous to that seen in epidermolysis bullosa.

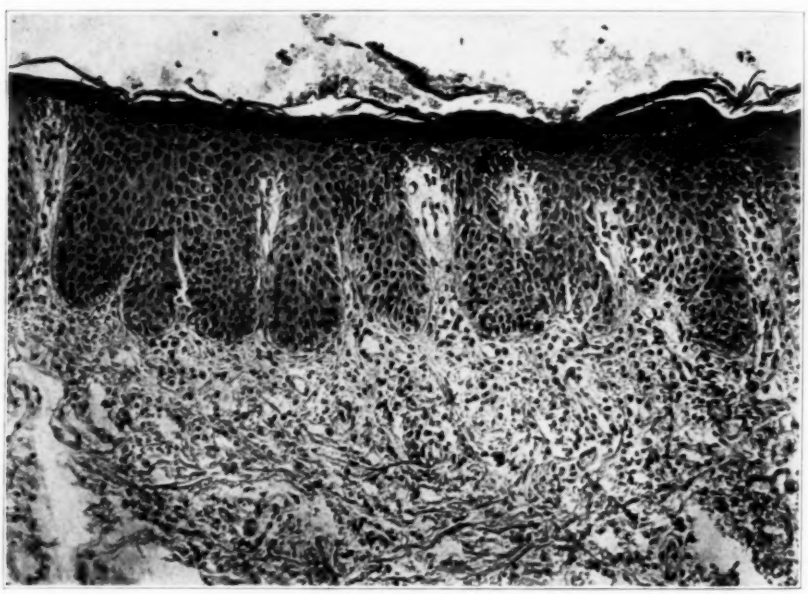

Fig. 7.—Section from the abdominal wall of first child, showing marked acanthosis, absence of horny layer and hyperactivity of stratum germinativum.

The epithelial changes herein described are not those ordinarily seen in congenital ichthyosiform erythroderma. It is noteworthy, however, that a fragmentation and reduction in the elastica has been noted in this disease as an occasional finding.

The complete absence of a pure hyperkeratosis as described by MacKee and Rosen for all of the cases and the elastica defect are the distinguishing histologic differences in the cases herein described from others of congenital ichthyosiform erythroderma.

COMMENT

In connection with the deficiency of the elastica in epidermolysis bullosa, Siemens,[3] who has made an exhaustive study of this disease, has lately expressed the opinion that this deficiency is not a primary or causative change. He states that it is not found in the nonatrophic form of epidermolysis bullosa, but is a characteristic finding of the dystrophic form. He concludes that the elastica is disorganized and absent as a result of the atrophic changes, and is therefore merely the expression of cutaneous atrophy.

Fig. 8.—Skin from the abdomen of a normal 3-year-old child for comparison.

The absence of all atrophy in the cases herein described and the existence of the characteristic elastic tissue changes, makes it seem possible at least that Engman and Mook's view regarding the elastic tissue change as primary and causative is still tenable.

Of more interest, however, than the histologic and clinical features of these cases, is the history of the familial occurrence of the group and particularly of the consanguineous marriage of the parents and the grandparents (Fig. 1).

3. Siemens: Zur klinischen Histologie und Aetiologie der sogenannten Epidermolysis bullosa traumatica, Arch. f. Dermat. u. Syph. **134**:454, 1921; Studien ueber Vererbung von Hautkrankheiten (Epidermolysis bullosa hereditaria), ibid. **138**:43, 1922.

The influence of heredity in the rôle of various cutaneous diseases has received little attention from the students of cutaneous medicine. The subject, however, has been studied in a most comprehensive and painstaking manner by Adrian [4] and latterly in a series of extensive monographs by Siemens.[5] This author has not only studied the influence of heredity on cutaneous malformations, but he has an excellent article on consanguineous marriage as influencing such conditions.

It is generally accepted that heredity plays a dominant or recessive rôle in the transference of abnormalities and malformation. If a disease is dominant, there is no latency in the parents, and it is transmitted

Fig. 9.—Showing deficiency, fragmentation and disorganization of the elastica of the subpapillary layer (Weigert's stain).

directly in an unbroken way from an affected parent to part of his children. Therefore, in dominant inheritance, it apparently makes no difference whether the affected parent marries a relative or a nonrelated person. In persons affected with a dominant inheritable disease, the probability of transmitting this to at least half of the descendants is always present, irrespective of the factor of consanguinity.

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4. Adrian: Die Rolle der Konsanguinität der Eltern in der Aetiologie einiger Dermatosen der Nachkommen, Dermat. Zentralbl. **9**:258, 1906.

5. Siemens: Ueber Vorkommen und Bedeutung der Gehaüften Blutverwandshaft der Eltern bei der Dermatosen, Arch. f. Dermat. u. Syph. **132**:206, 1921.

In recessive inheritance, however, the malformations or dystrophic changes exist in a latent form in the parents and forebears, and the issue or descendants of such persons are most apt to present the disease uncovered, or clinically when they receive the hereditary trait from both parents; that is, as in consanguineous marriage. Consanguineous marriage, therefore, is an etiologic factor in bringing out recessive inherited traits when the tendency is present in both parents.

Persons affected with a recessive type of malformation or disease when married to normal persons do not ordinarily transmit the disease to their children because of the tendency of the recessive trait to be covered by the normal parent. It is therefore not remarkable, as Siemens points out, in xeroderma pigmentosum so frequently found in brothers and sisters, that on the one hand, the parents are not affected, and on the other, the children of the affected persons are customarily free from the disease. Siemens' studies lead him to state that xeroderma pigmentosum, keratosis diffusa, albinism, and congenital ichthyosiform erythroderma are examples of cutaneous diseases and abnormalities in which recessive inheritance is definitely shown, and which are therefore influenced by their frequency in consanguineous marriage. To a lesser extent, palmar and plantar keratosis, ichthyosis vulgaris, the juvenile form of acanthosis nigricans, hydroa, Raynaud's disease, congenital hypertrichosis and hypotrichosis, granulosis rubranasi and certain onychauxes also fall into the group of inherited diseases in which the recessive factor is present.

Another most interesting phenomenon which is admirably brought out in the family tree of the group herein described is the question of sex limited inheritance. In recessive abnormalities, the condition is more commonly seen in males than in females. Furthermore, Siemens points out, it is seldom found from father to son, but is particularly often transmitted from the father to a grandchild through a daughter.

In my group of cases, the affected children acquired the disease through the paternal grandmother and the maternal grandfather, who were brother and sister. It is further of considerable interest in this group that a far larger proportion of the children are affected than is ordinarily seen, one to four being the usual ratio, whereas, in this group, three of four children are affected. All the affected children being males, the inheritance is therefore apparently sex limited in this family. Such sex limitations has been noted previously in ichthyosis serpentina, keratosis follicularis with hypotrichosis and in partial albinism of the hair. It is particularly a striking finding in congenital hypotrichosis. A few other conditions have been noted in which sex limitation occurs, but with such irregularity that they are not noted here.

Sex limitation in a dominant form of heredity cannot apparently be determined with any degree of certainty.

CONCLUSIONS

1. Herein are described three cases of congenital ichthyosiform erythroderma of an unusual type.

2. Clinically they are characterized not by true ichthyosis, but by a scarlatinal form of exfoliation.

3. Histologically, they are characterized by acanthosis, fragmentation and disorganization of the elastica of the upper layers of the cutis.

4. The group is further characterized by a striking history of consanguineous marriage as probably the predisposing factor of a recessive type of inherited dystrophy.

5. The affection having occurred exclusively in the male children, indicates that the group is an example of sex limitation in recessive inheritance.

6. The histologic similarity of the cases to the fundamental changes of epidermolysis bullosa of the dystrophic form, together with the fact that both diseases are recessive in their inheritance, suggests a close relationship between the two.

DUODENAL LAVAGE IN THE TREATMENT OF JAUNDICE COMPLICATING THE TREATMENT FOR SYPHILIS *

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Since the introduction of the duodenal tube by Gross, in 1911, many indications for its use have been proposed. Like all innovations in the medical world, it soon became a panacea. It was used in the treatment of diabetes, chronic duodenal catarrh, cholelithiasis, chronic icterus,[1] malnutrition, gastroptosis, persistent vomiting, duodenal ulcer,[2] gastric ulcer,[3] indicanuria, seborrhea of the face, spasms of the larynx, chronic bronchitis, chronic gastro-enteric catarrh, constipation,[4] chronic intestinal parasitic disease, oxyuris, achylia pancreatica,[5] amebic dysentery, sciatica, melancholia, dementia, ptomaine poisoning, exophthalmic goiter, paroxysmal tachycardia, mucous colitis, psoriasis,[5] chronic arthritis,[6] pylorospasm, hypersecretion, hyperemesis gravidarum, gastric atony, arteriosclerosis, epilepsy, nephritis, neuralgia, neuritis, anemia, insomnia, anorexia, and catarrhal jaundice,[7] in all of which it was employed with a measure of success. Lyon,[8] Einhorn,[9] and Weilbauer [10] emphasize its

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1. Gross, M. H.: Direct Lavage of the Duodenum, New York M. J. **93**: 171-172, 1911.

2. White, F. W.: Observations on the Use of the Duodenal Tube for Diagnosis and Treatment, Boston M. & S. J. **174**:710-715, 1916.

3. Aaron, C. D.: The Therapeutic Value of the Duodenal Tube, New York M. J. **116**:648-651, 1922. Rosenberger, F.: Ueber Duodenaltherapie, Med. Klin. **9**:1249-1251, 1913.

4. Jutte, M. E.: Transduodenal Lavage. Treatment and Report of Some Cases of Chronic Diseases, J. A. M. A. **60**:586-587 (Feb. 22) 1913; Autointoxication Treated by Duodenal Lavage, Am. J. M. Sc. **153**:732-738, 1917.

5. Levin, A. L.: Transduodenal Lavage, New Orleans M. & S. J. **72**: 263-270, 1920.

6. Simon, S. K.: The Direct Aspiration of the Contents of the Biliary Tract Through the Duodenal Tube. Clinical Application and Therapeutic Possibilities of the Method, South. M. J. **14**:447-455, 1921.

7. Churchill, J. F.: The Use of the Duodenal Tube, J. Iowa State M. Soc. **6**:17-21, 1916.

8. Lyon, B. B. V.: The Treatment of Catarrhal Jaundice by a Rational, Direct and Effective Method, Am. J. M. Sc. **159**:503-512, 1920; Non-Surgical Drainage of the Gall-Tract, Philadelphia, Lea & Febiger, 1923.

9. Einhorn, M.: The Duodenal Tube as a Factor in the Diagnosis and Treatment of Gallbladder Disease, J. A. M. A. **66**:1908-1910, 1916.

10. Weilbauer, A.: Praktisches und Kritisches zur duodenal Sondiering, Klin. Wchnschr. **1**:2512-2515, 1922.

indication as a diagnostic aid in the more direct examination of fresh duodenal content. This examination includes physical, chemical and microscopic tests. Catarrhal jaundice,[11] and the various gallbladder [12] and biliary affections [13] seem especially suitable for duodenal treatment.

During the last two years I have made a special study of duodenal lavage in the treatment of jaundice which complicated the treatment for syphilis; it was not used for diagnostic purposes. While the etiology of the jaundice was not especially studied in this series, it seems probable, as was pointed out by Stokes, Ruedemann and Lemon,[14] that there is a definite infectious factor in many of these cases, independent of a possible lowered resistance of the liver from treatment for syphilis. Most of the cases are of the simple cholangitis type, and respond readily to treatment. Occasionally a rather severe type of toxic hepatitis, even terminating in acute yellow atrophy of the liver, is encountered.

There were thirty-three patients in the series, twenty-nine men and four women. The ages varied from 20 to 62 years, the average being 40.6 years. Twenty of the patients had neurosyphilis; two visceral, one ophthalmic, one cutaneous, two vascular, one osseous, two latent, and three early syphilis; one had nonsyphilitic meningo-encephalitis.

The average duration of the syphilitic infection in twenty-four patients was sixteen and one-half years, ranging from six months to thirty years. They had received various antisyphilitic treatments previous to the development of jaundice: twenty-one had been given arsphenamin, mercuric succinimid and potassium iodid, eleven arsphenamin and mercury, and one mercury and iodids.

Nine of the thirty-three patients gave a definite history of intercurrent infection: three had urticaria, two sore throat, three arthritis and one "cold." No epidemic factors were elicited, most cases occurring during or shortly after a course of mercurial inunctions, and in all months of the year except December and January; the greatest number occurred in February and August. The symptoms complained of were

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11. Hopkins, A. H.: The New and Direct Method of Treating Catarrhal Jaundice, New York M. J. **115**:710-711, 1922. Ousley, J. W.: Duodenal Lavage in Treatment of Catarrhal Jaundice. Case Report, South M. Jour. **12**:597-599, 1919; also footnote 8.

12. Levin, A. L.: Medical Treatment of Gallbladder Diseases Versus Surgical, New Orleans M. & S. J. **73**:252-258, 1921.

13. Meakins, J.: Duodenal Tube in Biliary Diseases, Brit. M. J. **1**:983-987, 1922. Rehfuss, M. E.: Medical Treatment of Biliary Affections, M. Clin. N. Am. **2**:815-828, 1918-1919.

14. Stokes, J. H.; Ruedemann, R., Jr., and Lemon, W. S.: Epidemic Infectious Jaundice and Its Relation to the Therapy of Syphilis, Arch. Int. Med. **26**:521-534 (Nov.) 1920.

those commonly associated with jaundice: thirty-one were nauseated, thirty had lost appetite, twelve vomited, eleven were apathetic, seven had pain in the abdomen and three had ascites with edema.

The treatment is essentially that outlined by Lyon. The duodenal tube is passed into an empty stomach according to the usual method,[15] and the stomach washed until the return fluid is perfectly clear. When the tube is in the duodenum, the latter is washed first with water at 40 C., then about 100 c.c. of saturated solution of magnesium sulphate is washed back and forth in a syringe with a capacity of 100 c.c. for about ten minutes. The duodenal contents are then allowed to siphon out. This process is repeated three or four times, at intervals of thirty minutes. The tube is then withdrawn, the stomach being washed again at this time. The tubing is repeated every other day. From one to eight tubings were used in this series of cases.

Practically all of the patients were placed on sodium acid phosphate. Oxgall tablets were given at the same time in an effort to apply the observations of Eppinger [16] on the effect of this substance in diminishing the viscosity of the bile in cholangitis. Two thirds of the patients were given a course of calomel and a saline purgative once or twice during the course of treatment. In only a few of the severer cases the patients were given glucose solution by proctoclysis.

The diet was rich in carbohydrates and fresh fruits. Special attention was paid to the individual patient's craving for particular foods. The fresh fruits are usually craved. Milk, eggnog and toast are especially desirable. The use of meat is discouraged, and the patient seldom asks for it.

The response to duodenal lavage by patients who have failed to improve under the ordinary medical treatment is usually remarkable.

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15. The tip of the tube is placed on the tongue, close to its base and the patient is told to swallow. During the act of swallowing, the tube is gently started down the esophagus, and is passed until a level of about 50 cm., midway between the first and second markings, is reached. At this level the stomach is washed with sterile water until the return is clear. The patient is then instructed to lie on his right side, extending his right leg and acutely flexing his left knee and hip. He is told to pass the tube at the rate of 1 inch every five minutes until the third mark (75 cm.) is reached. We know that the tube is in the duodenum by a change in reaction of the aspirated fluid from acid to alkaline; by the character of the duodenal juice, which is usually a pearly viscid fluid in which floccules are suspended; sometimes by the presence of bile; by a slight tug when the tube is pulled gently, and by seeing the tip beyond the pylorus at fluoroscopic examination. The tube is removed by withdrawing it gently until the tip reaches the nasopharynx; the patient is then told to swallow, and the tip is easily recovered.

16. Eppinger, H.: Weitere Beiträge zur Pathogenese des Ikterus, Beitr. z. path. Anat. u. z. allg. Path. **33**:123-157, 1903; Ikterus, Ergebn. d. inn. Med. u. Kinderh. **1**:107-156, 1908.

A man who has eaten but little for weeks and has vomited even water, will eat a fairly generous meal and really enjoy it. In thirty of the thirty-three patients the nausea disappeared permanently. Twenty-eight patients recovered their appetite. Nine of the twelve patients who had vomited previous to the lavage ceased vomiting. Five of seven patients were relieved of the abdominal pain. Cheerfulness replaced the apathy in seven of eleven patients. Thus practically all of the symptoms were relieved.

ILLUSTRATIVE CASES

Case 1.—A man, aged 26, who came to the Clinic, had primary syphilis. His first course of treatment consisted of eight intravenous injections of arsphenamin, twenty-five injections of mercuric succinimid intramuscularly, and four injections of mercuric salicylate, followed, after one month of rest, by sixty mercurial inunctions. About fourteen weeks after the course of arsphenamin, the patient returned to the Clinic markedly jaundiced. He was hospitalized and the usual treatment instituted. After 2 grains (0.1 gm.) of calomel in divided doses, the duodenum was lavaged, three times, on alternate days; this resulted in cessation of the nausea and vomiting, and return of appetite and cheerfulness; alertness replaced the toxic state. The patient was given oxgall and effervescent sodium phosphate. He was dismissed from the hospital six days after admission, but two days later had a recurrence of nausea, vomiting and hiccup. One duodenal lavage produced remarkable symptomatic improvement. It marked the turning point in the patient's recovery. Nausea and vomiting ceased, and his appetite and general condition improved materially. Marked edema of the ankles persisted. One week later he was again dismissed from the hospital. A low protein diet, restricted fluid intake, oxgall tablets and magnesium sulphate were continued. His condition steadily improved, and six weeks after admission he was dismissed from the Clinic. Fourteen days later he resumed work. Fourteen weeks later he returned to the Clinic in excellent condition, the jaundice and edema having entirely subsided. He was then given a Pollitzer course of arsphenamin, that is, three intravenous injections in as many days, without incident, a fact which certainly suggests that arsphenamin could hardly have been responsible for the previous hepatitis.

Comment.—Duodenal lavage helped materially in overcoming this resistant jaundice. The patient's condition steadily declined under ordinary treatment, while with the last lavage an uneventful recovery began.

Case 2.—A man, aged 52, entered the Clinic, in July, 1922, and a diagnosis of late neurosyphilis (tabes dorsalis) was made. He received eight intravenous injections of arsphenamin, thirty intramuscular injections of mercuric succinimid and twenty-two intravenous injections of sodium iodid. Six weeks later he was dismissed from the Clinic, and instructed to take forty mercurial inunctions at home. Five months later he returned for more vigorous treatment. This time he received twelve intravenous injections of arsphenamin, combined with three intraspinal treatments according to the Swift-Ellis-Ogilvie technic, and twenty intramuscular injections of mercuric succinimid and twenty-one intravenous injections of sodium iodid. At the end of this course of treatment, he complained of progressive numbness in the hands and feet, which was thought to be due to arsenical neuritis; four injections of sodium thiosulphate were

given. On Feb. 21, 1923, he was allowed to go home. One week later he returned, complaining of numbness all over his body, and arthritic and myalgic pains. Three days later he developed definite jaundice. A course of calomel followed by magnesium sulphate was given preparatory to duodenal lavage. Eight duodenal lavages were given; but not until the sixth lavage, three weeks after the onset of jaundice, was there a satisfactory drainage of bile. The patient failed to improve until a free drainage was obtained, showing that merely washing the stomach has no effect. Following successful duodenal lavage, the nausea and vomiting ceased, the appetite returned and the patient regained his normal mental alertness. Seven weeks after the onset of jaundice he developed edema of the thighs and scrotum, which subsided markedly on digitalization. Ten weeks after the appearance of jaundice, he was allowed to go home. The edema was rapidly subsiding. At the end of two months, he wrote that the jaundice and ascites had entirely disappeared.

Comment.—This was another case of resistant jaundice in which there was probably extensive hepatic damage. The improvement definitely followed successful duodenal lavage; merely washing the stomach had no effect on the jaundice.

Case 3.—A woman, aged 58, entered the Clinic in March, 1921, complaining of debility. A diagnosis of aortic aneurysm was made, and treatment for syphilis instituted. The patient was hospitalized, and was given five injections of neo-arsphenamin intravenously, forty mercurial inunctions, and potassium iodid by mouth. Two months after admission, she was dismissed with instructions to take mercury with chalk at home. At the end of three months, she returned to the Clinic. She was advised to take two courses of forty mercurial inunctions at home. Her next visit to the Clinic was made in March, 1922, when she received ten intravenous injections of sodium iodid and twenty-one intramuscular injections of mercuric succinimid. Two months later, she was dismissed with instructions to take potassium iodid, and forty mercurial inunctions at home. Four months after her previous admission, she returned to the Clinic complaining of pain below the right costal margin, nausea and vomiting. The sclerae and skin showed a definite icterus. She had received no arsphenamin for fourteen months, which tends to exclude an arsenical basis for the jaundice. The first duodenal lavage was unsatisfactory, owing to lack of cooperation on the part of the patient. Even the slight lavage obtained seemed to produce definite symptomatic improvement. The nausea and vomiting soon recurred, however. She was given a course of calomel and magnesium citrate with no relief. She refused to take food and even water because it aggravated the nausea. Nine days after the first attempt, another duodenal lavage was given, much to the patient's displeasure, but with satisfactory results. The tube was left in situ, and five feedings of 250 c.c. of sweetened eggnog were given at three hour intervals. This is a valuable procedure for patients with debility due to lack of nourishment. At noon of the second day the tube was removed. This was the turning point in this patient's illness also; the transformation was almost miraculous. She was much more cheerful, the nausea and vomiting disappeared, appetite returned, and she left her bed for the first time in seven days. Improvement continued steadily. A course of potassium iodid and forty mercurial inunctions were now given, followed by a course of six intramuscular injections of sulpharsphenamin, without incident. Recently the patient recommended duodenal lavage to a friend with jaundice.

Comment.—Duodenal lavage produced a rapid and remarkable improvement in this patient, after the usual treatment had absolutely failed. This was the most striking recovery following duodenal lavage in the series, and emphasizes the value of combining duodenal feeding with lavage for debilitated patients.

Case 4.—A woman, aged 30, entered the Clinic in October, 1922, complaining of swelling of both sides of the neck. A diagnosis of gumma of the lymph nodes was made. She was given a course of treatment for syphilis, consisting of six intravenous treatments of arsphenamin, twenty-seven intramuscular injections of mercuric succinimid and potassium iodid by mouth. She was dismissed from the Clinic six weeks after admission, after having been advised to take potassium iodid and forty mercurial inunctions during the next four months. On her return to the Clinic, she complained of early morning nausea and vomiting, loss of appetite, and pain in the upper right side of the abdomen. She thought that she might be pregnant. She was given one intravenous injection of arsphenamin. Three days later a definite icterus, the prodrome of which had caused the symptoms complained of, became evident. She was immediately hospitalized and duodenal lavage on alternate days instituted. Two lavages failed to obtain bile. The condition of the patient was not progressing favorably, and she became markedly toxic. The third lavage recovered an unusually large amount of bile, and proved the turning point in recovery. The nausea, vomiting and pain in the abdomen disappeared, the appetite returned, and the patient's normal mental alertness was restored. Her recovery was uneventful and complete. Nineteen days after the onset of jaundice, five intramuscular injections of sulpharsphenamin at weekly intervals and fourteen intramuscular injections of mercuric succinimid were given without incident. Evidently the etiology of the jaundice was not arsenical. On June 4, the patient was dismissed with the interim treatment of forty mercurial inunctions. On September 17, she returned, and completed another course of treatment, consisting of six intravenous injections of arsphenamin and twenty-seven intramuscular treatments of mercuric succinimid, without incident.

Comment.—Marked immediate symptomatic improvement followed the first successful duodenal lavage in this case, and terminated in complete recovery, after the usual measures had failed.

Case 5.—A man, aged 60, entered the Clinic in May, 1922. A diagnosis of late neurosyphilis of the meningovascular type was made, and he was placed on treatment for syphilis, consisting of thirty-four intramuscular injections of mercuric succinimid. At the end of two months he was dismissed from the Clinic, being instructed to take mercurial inunctions and potassium iodid by mouth after a rest interval of thirty days. He returned to the Clinic six months later, with a jaundice of ten weeks' duration. He had received no arsenical treatment previous to this time. The jaundice had become deeper during the last week under the usual type of medical treatment. The only complaint was marked pain in the upper right side of the abdomen. The liver margin was definitely palpable. The patient received oxgall tablets by mouth, a course of calomel followed by magnesium sulphate and duodenal lavage. Only one lavage was given, but the results were excellent. It marked the beginning of the patient's complete recovery. The pain in the right upper quadrant

entirely disappeared. The jaundice continued to clear up, and ten days after this, neo-arsphenamin was started intravenously. The patient was dismissed six weeks after admission, entirely recovered from the jaundice.

Comment.—Duodenal lavage was the deciding factor in this patient's complete recovery, again proving successful when ordinary measures had failed. This case also tends to eliminate arsenic as the etiologic factor in producing this type of jaundice.

CASE 6.—A man, aged 42, entered the Clinic in November, 1921. A diagnosis of tabes dorsalis was made. The patient went home for treatment and returned in April 22, 1922, having had six intravenous injections of neo-arsphenamin and thirty-five mercurial inunctions elsewhere. He was given five intravenous injections of arsphenamin, two intraspinal treatments according to the Swift-Ellis-Ogilvie technic, twenty intramuscular injections of mercuric succinimid, and eleven intravenous injections of sodium iodid. Ten weeks later, he complained of pains all over his body and lightning pains from his waist down to his feet. Combined intravenous and intraspinal arsphenamin treatment and intramuscular injection of mercuric succinimid was resumed. Sixteen days later he developed definite early jaundice of which the foregoing complaints were prodromal. He manifested a marked anxiety neurosis, and was immediately hospitalized. Three successful lavages on alternate days were accomplished. Nine days after the onset of the jaundice, the patient was dismissed from the hospital. The nausea had ceased following the first lavage; his appetite improved, and normal mental equilibrium was restored. Treatment for syphilis was resumed immediately. Five intravenous injections of arsphenamin, three intraspinal treatments, and twelve intramuscular injections of mercuric succinimid were given without incident. Since then four injections of arsphenamin and sixteen of mercuric succinimid have been given. There has been no recurrence of jaundice.

Comment.—Successful duodenal lavage resulted in immediate and continued improvement of the patient's condition. The immediate resumption of arsphenamin without ill effect indicates that the hepatic process could scarcely have been arsenical in origin.

SUMMARY

Thirty-three patients were treated by duodenal lavage, thirty (90 per cent.) of whom, recovered definitely and rapidly following this procedure. A maximum of eight lavages, and an average of two, was necessary for relief. The average duration of toxic manifestations was from ten to twelve days.

Duodenal lavage is a valuable adjunct in the treatment of jaundice from toxic or infectious cholangitis complicating treatment for syphilis; it controls the nausea and vomiting, restores the appetite, relieves the abdominal pain and clears up the toxic mental state. Only the most severe cases of jaundice of this type fail to respond in some degree to duodenal lavage.

After a successful duodenal lavage in cases of infectious cholangitis, treatment for syphilis may be cautiously resumed. Lavage should be repeated on alternate days until bile is obtained, and should be continued until the patient's symptoms are entirely relieved.

The cases cited tend to show that arsenic is not necessarily the etiologic agent that produces this type of jaundice.

MERCURIAL ERUPTIONS

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Eruptions following the use of mercury are not common, considering the widespread use of the drug, yet a review of the literature reveals the fact that the occasional dermatoses which do result from its use are almost as varied in their morphology as the eruptions which may occur after the use of arsphenamin. Since the introduction of the organic arsenicals in the treatment of syphilis, a voluminous literature has collected on the eruptions which may follow their use, and but scant attention has been paid to the eruptions which may occur after the use of mercury. A notable exception is a comprehensive monograph by Almquist.[1] A review of the American literature of the past twenty years reveals scarcely a mention of mercurial eruptions. This is surprising in view of the fact that the possible cutaneous manifestations from this drug parallel in part those of arsphenamin.

Mercury may evoke eruptions either by local irritation or through absorption. Thus, eruptions may result from external applications, from ingestion, from hypodermic injection and even from inhalation. External applications undoubtedly call forth the majority of cutaneous manifestations, although when due to the external applications of mercury the eruption is generally limited to the areas treated. An exception to this is seen in the following case, which illustrates how severe a mercurial eruption may be:

CASE 1.—*History.*—A man, aged 28, had been advised by a pharmacist to apply blue ointment locally for pediculosis pubis. One application only was made to the pubic region and groins. Within a few hours there developed an itching of the entire body and a reddening and slight vesiculation of the skin of the penis, scrotum and groins. No further application of the blue ointment was made, but within forty-eight hours after the first application the entire body presented a scarlatiniform appearance, and the itching became intense, so much so that the patient was unable to sleep. It was on the fourth day that I was called in consultation.

Examination.—The entire cutaneous envelop presented a diffuse erythematous eruption. There was some edema of the eyelids and cheeks, and marked edema of the penis and scrotum, associated with superficial vesiculation. Clinically, the picture resembled that of an erythrodermia following the use of arsphenamin. The patient was in a state of marked excitation, and was unable to refrain from continuous scratching. The temperature was slightly elevated. There were no other manifestations of mercurial poisoning, except a slight albuminuria.

1. Almquist: Arch. f. Dermat. u. Syph. **141**:343, 1922; Acta dermato-ven. 3:106, 1922.

Outcome.—On account of the excited state of the patient and intense pruritus, a sedative was prescribed, and locally starch and soda baths and a simple calamin lotion were used. Although the pruritus continued for a period of about two weeks with a gradually decreasing intensity, the eruption disappeared in a single week. The patient was warned against the further use of preparations of mercury.

The cutaneous manifestations resulting from the use of mercury are classified by Almquist as (1) toxic dermatoses or (2) artificial dermatoses of chemical origin. The clinical pictures of the eruptions are not diagnostic per se. There is no definite location; they may appear at the sites of application or far removed from them. In cases resulting from internal administration, Almquist has observed that in more than 50 per cent. the first manifestations occur on the cooler parts of the body, such as the buttocks, hands and feet and over the tibiae.

CLINICAL PICTURES OF ERUPTIONS RESULTING FROM THE USE OF MERCURY

As stated previously, only in rare instances can a diagnosis of mercurial eruption be made from the clinical examination. Diagnosis usually rests on the history, unless there is local evidence of mercury having been used, such as might result from inunctions of blue ointment. A variety of dermatoses may be simulated, as the following list compiled from the literature of the past half century reveals: Folliculitis or acne mercurialis, eczematoid eruptions, morbilliform eruptions, scarlatinoid eruptions, erysipeloid eruptions, purpura hemorrhagica, erythema exudatatium multiforme, pemphigoid eruptions, exfoliative dermatitis, urticaria, varioliform eruptions, herpes zoster, pigmentation and exanthems. To this formidable list might be added pruritus, as evidenced by a personal case of which mention will be made later.

Folliculitis or Acne Mercurialis.—This is the most frequent eruption resulting from mercury and occurs from the use of inunctions. Localized to the hairy portions of the body, it is most common on the regions where the hair is most abundant. Even though the patient may be instructed to avoid the hairy portions of the body, this is not always possible unless a masseur be employed to make applications to the back, which is almost universally free from considerable hairy growth. It is not advisable to shave the parts to be rubbed, for this merely removes the surface hair and does not lessen the tendency to involvement of the follicles.

According to Tomaszewski,[2] several factors play a part in the development of this folliculitis: (1) the amount of hair present, (2) the mode of application, (3) the composition of the ointment used, and (4) the bacterial flora of the skin.

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2. Tomaszewski: Ztschr. f. klin. Med. **51**:439, 1904.

Clinical Picture: At the site of the applications of mercury there appear a few or many papular lesions. These are usually infiltrated, conical, slightly inflammatory elevations, all of which are situated about the hair follicles. These lesions may spontaneously disappear or may become secondarily infected and suppurate. In the latter event, small pustules, abscesses or phlegmons result. It is a moot question whether the primary lesions of a mercurial follicular eruption contain organisms. Sabouraud (quoted by Tomaszewski) is of the opinion that staphylococci are etiologic factors in their production, while Frederic (also quoted by Tomaszewski) holds that the contents of the primary papules are sterile.

It is doubtful whether this type of eruption ever results from the internal administration of mercury, although Rosenthal [3] reported the case of a soldier who developed acneform lesions on the legs and arms following injections of mercurial salicylate.

Eczematoid Eruptions.—Eruptions having the clinical aspects of an eczema may result from either the external application or the internal administration of mercury. When due to the external use of mercury, they usually start as a dermatitis venenata. The common sites for eruptions of this type are the axillae and groins. Cases of localized dermatitis of the scrotum, penis and groins are common after the application of blue ointment for pediculosis pubis, giving evidence of the extreme sensitiveness of this region to mercury. It is not uncommon for a patient applying inunctions to the arm or flank in treating a syphilitic infection, to anoint a sufficiently generous amount to include the axillae or groin. The combination of heat, profuse perspiration and an irritating ointment may then result in the production of a dermatitis. Such a development results in marked symptoms of burning and intense discomfort from the local inflammation set up.

The true mercurial eczemas result from the absorption of the drug, although an acute dermatitis may undergo transition into an eczema. The differentiation is purely an arbitrary one. Transition from a simple erythema may result in the production of a papulovesicular or papulopustular injection, and in rare instances hemorrhagic lesions may occur. Individual lesions may coalesce to form patches which in turn coalesce to form larger patches until in extreme cases the entire body may be involved, including, in rare instances, the hair and nails. The nails have been observed to become fissured, rough, brittle and to fall out.

The other forms of mercurial eruptions are rare, and only isolated instances appear in the literature. Some of the cases are of sufficient interest to warrant a brief report.

3. Rosenthal: Berl. klin. Wchnschr. **32**:500, 1895.

Morbilliform Eruptions.—Morbilliform eruptions have been reported by Ferrand [4] as developing after inhalations of mercury, by Brouardel and Ogier [5] after the accidental ingestion of large doses of mercuric sulpho-cyanid and mercuric nitrate, and by Auer [6] after the taking of a small amount of sublimate by mouth. Tomaczewski reported the case of a girl who developed a morbilliform exanthem accompanied by a high temperature, conjunctivitis, rhinitis and bronchitis after four injections of mercury thymol acetate. After the eruption disappeared, a fifth injection of the drug was given and was followed by a reappearance of the eruption and symptoms, thus proving that the mercury was entirely responsible.

Scarlatiniform Eruptions.—Examples of scarlatiniform eruptions occurring after mercury are more numerous. Cases have been reported by Alexander,[7] Bossard,[8] Eich,[9] Allgeyer and Sprecher [10] and others. In the case of Allgeyer and Sprecher, the scarlatiniform eruption followed sublimate injections.

Erysipeloid Eruptions.—Eruptions simulating erysipelas are described in cases reported by Englemann,[11] Fournier,[12] Kriedmann [13] and others. In Englemann's case, a bright erythematous eruption developed on the face, within twelve hours after taking calomel by mouth. The eruption was associated with local edema and a temperature of 104 F. At a later date, after the first eruption had completely involuted, a similar condition was produced by the ingestion of pills containing mercury.

Purpura Hemorrhagica.—Fournier [14] reported a case in which a purpuric eruption appeared following the ingestion of VanSwieten's liquor, and Rosenthal [15] and Fischkin [16] reported cases in which purpuric lesions followed inunctions. Other cases of purpuric eruptions following the use of mercury have been reported by Buertzeff,[17] Friedheim [18] and Suygen.[19]

4. Ferrand: Union Med., No. **32**:401, 1868.
5. Brouardel and Ogier: Ann. d'Hyg. pub. **29**:352, 1893.
6. Auer, quoted by Bossard: Dermat. Ztschr. **55**:50, 1897.
7. Alexander: Arch. f. Dermat. u. Syph. **16**:105, 1884.
8. Bossard: Dermat. Ztschr. **4**:50, 1897.
9. Eich: Therap. Monatschr., 1894, p. 496.
10. Allgeyer and Sprecher: Deutsch. med. Wchnschr. **38**:636, 1895.
11. Englemann: Berl. klin. Wchnschr. **43**:647, 1897.
12. Fournier: Ann. de dermat. et. syph., 1893, p. 272.
13. Kriedmann: Boston M. & S. J. **7**:18, 1898.
14. Fournier: Ann. de dermat. et. syph., 1898, p. 564.
15. Rosenthal: Berl. klin. Wchnschr., Nos. 23 and 24, 500 and 524, 1895.
16. Fischkin: J. Cutan. Dis. **23**:182, 1905.
17. Buertzeff: Abst., Brit. J. Dermat., 1886, p. 811.
18. Friedheim: Dermat. med Wchnschr., No. 11, 182, 1895.
19. Suygen: Brit. M. J., April, 1905.

Erythema Multiforme Exudativum.—Bonnet [20] has reported a case of erythema multiforme of the iris type which occurred after taking mercury, and in which a second attack was later produced by again giving the drug. Cases have also been reported by Rosenthal, Calloman,[21] DuMesnil [22] and others.

Pemphigoid Eruptions.—Instances of eruptions simulating pemphigus have been reported as occurring after the use of mercury by Belmer,[23] Frankel,[24] Mouflier,[25] Petrini,[26], Thimm [27] and others. In some of these cases, the eruption was benign, recovery occurring on cessation of the mercurial therapy. Such cases may be allied to the erythema multiforme group.

Exfoliative Dermatitis.—Such cases usually follow either a preliminary mercurial erythema or a diffuse dermatitis, and are in most instances the result of maltreatment. The appearance of a diffuse erythematous or scarlatiniform eruption during a course of mercurial therapy should be a warning sign to discontinue medication, just as it would be if developing after treatment with arsphenamin. Among those reporting cases of exfoliative dermatitis following the use of mercury may be mentioned Milian,[28] Beck,[29] Blanc [30] and Touton.[31]

Uticarial Eruption.—Urticaria occurring after the use of mercury has been described by DuMesnil, Herxheimer,[32] Friedheim, Hoffman and others.

Varioliform Eruption.—An isolated case of a varioliform following mercurial treatment has been described by Guelpa.[33]

Herpes Zoster.—Touton [31] reported a case in which a herpes zoster developed in a patient receiving mercury. The relationship is questionable.

Pigmentations.—Almquist states that pigmentation of the skin may result from long continued treatment with mercury. I found no reference to cases in which this occurred in the literature.

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20. Bonnet: Lyon med. **107**:457, 1906.
21. Calloman: Dermat. Ztschr. **8**:407, 1901.
22. Du Mesnil: München. med. Wchnschr. **28**:465, 1888.
23. Belmer: Dermat. Ztschr. **8**:13, 1901.
24. Frankel: Monatschr. f. prakt. Dermat. **43**:720, 1901.
25. Mouflier: Union Med., 1891, p. 377.
26. Petri: Ann. de dermat. et syph., 1891, p. 223.
27. Thimm: Dermat. Ztschr. **9**:782, 1902.
28. Milian: Ann. de dermat. et syph., 1898, p. 167.
29. Beck: Berl. klin. Wchnschr., No. 7, 153, 1896.
30. Blanc: Provinc. med. Lyon **2**:393, 1887.
31. Touton: Arch. f. Dermat. u. Syph. **21**:775, 1889.
32. Herxheimer: Therap. Monatschr., 1896, p. 77.
33. Guelpa: Jour. des mal. cutan. et syph. **1**:39, 1889-1890.

Enanthems.—Mercurial exanthems may in occasional cases be accompanied by an enanthem. DuMesnil [22] has described an enanthem localized in the buccal cavity, and Hoffman [34] described an enanthem involving the buccal cavity, pharynx, conjunctiva and the genital mucosa. Even the mucous membrane of the ureter showed an enanthem in a case which came to necropsy and later was reported by Loiano.[35]

To the cutaneous manifestations already listed may be added pruritus, which occurred in a case that I saw following injections of mercury.

CASE 2.—A woman, aged 45, obese, had received a series of arsenical injections for a latent syphilis, and after one month's rest was advised to take a series of mercurial injections. The first injection consisted of 1 grain (0.06 gm.) of mercuric salicylate, intramuscularly. The day following she reported a severe itching of the entire body. Examination was entirely negative; so she was given a placebo and advised to return in two weeks. At the termination of this period, she again presented herself at the clinic and said that the pruritus had almost disappeared, although it had been present constantly since the previous visit. She was persuaded to take another salicylate injection, and this time one-half grain (0.03 gm.) was given. A flare-up of the pruritus resulted, and the patient was then transferred to bismuth therapy, with good results. Unfortunately, a complete study was not made at the time, with a view of seeking out the cause of this unusual reaction.

MARKED IDIOSYNCRASY TO MERCURY

Some cases reveal a marked idiosyncrasy of the patient to the drug and are worthy of special mention. Schnell [36] reported a case in which a single inunction produced a generalized erythema, which is similar to my Case 1. DuBreiulh [37] described a case in which a scarlatiniform erythema occurred after the internal ingestion of 0.05 cg. of calomel. A patient of Bossard [38] developed an erythema after two doses of 0.05 cg. of calomel. In Gaucheraud's [39] case, a generalized erythema resulted from the ingestion of one Depuytren pill.[40] Recently a case has been reported by La Borde [41] of a prostitute who developed a generalized erythema after an injection of one-sixth grain (0.01 gm.) of biniodid of mercury, and who eventually died of mercurial poisoning.

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34. Hoffman: Berl. klin. Wchnschr., 1902, p. 908.
35. Loiano: Monatschr. f. prakt. Dermat. **36**:271, 1903.
36. Schnell: Abst., Monatschr. f. prakt. Dermat. **16**:44, 1893.
37. Du Breiulh: Ann. de la policlin. de Bordeaux **1**:48, 1889.
38. Bossard: Dermat. Ztschr. **70**:50, 1897.
39. Gaucheraud: Thèse, Paris, 1886.
40. According to Fournier, a Depuytren pill contains mercuric chlorid, 1 cg.; extract of opium, 2 cg., and extract of guaiacum, 4 cg.
41. La Borde: Ann. de dermat. et syph., 1922, p. 425.

PATHOGENESIS OF MERCURY EXANTHEMS

The theories as to the pathogenesis of eruptions following the administration of mercury are widely varied. Of course, the follicular eruptions which occasionally follow mercury applied locally may be explained on a purely local chemical basis. In regard to the other eruptions, the matter is not so simple to explain. Lesser [42] suggested that they might be of "nervous" origin. Rosenthal [43] was the first to suggest that the patients affected might have an idiosyncrasy for the drug. This view has since had many supporters. Peters [44] more recently has gone a step further and associated the idiosyncrasy in every case with a peculiarity of the surface epithelium, whether the eruption was of exogenous or endogenous origin. Lewandowsky [45] believes that the erythema is due to a vascular injury and the eczema to an epithelial injury.

The most extensive study of mercurial eruption is that of Almquist. According to this writer, mercury circulating in the blood stream of a susceptible person leads to a paralysis of the sympathetic nerves and a resultant dilatation of the blood vessels and edema. The conditions then are favorable for the growth of bacteria, and this is soon followed by leukocytosis. Almquist believes that the mercury acts only to give the initial impulse, for he has observed eruptions following the use of the drug continue for months after all the mercury had been eliminated.

Hoffman found that the blood showed an increase in leukocytes following the development of a mercurial eruption, and there was a marked eosinophilia. Even the mildest erythema showed the increase in eosinophils, while in some severe eruptions there was an eosinophilia of from 40 to 50 per cent.

TREATMENT

In many cases, merely stopping the use of mercury suffices for a clearing up of the cutaneous manifestations. A localized dermatitis may be treated with simple compresses of boric acid solution or with applications of calamine lotions. When there is a generalized erythrodermia with severe pruritus, sedatives may be necessary in addition to external remedies. It is usually a peculiarity of mercurial eruptions that they are unassociated with other signs of mercurial intoxication (stomatitis, colitis, etc.). However, should there be evidence of general mercurial poisoning, treatment should be directed toward a rapid elimination of the mercury.

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42. Lesser: Dermat. med. Wchnschr., No. 14, 286, 1888.
43. Rosenthal: Berl. klin. Wchnschr., No. 24, 500, 1895.
44. Peters: Dermat. Ztschr., 1918, p. 72.
45. Lewandowsky: Cor.-Bl. f. schweiz. Aertzte **48**:371, 1918.

SUMMARY

In conclusion, it may be stated that mercury may call forth almost as many cutaneous reactions as arsphenamin, and it is well to bear this in mind when a patient receiving mixed treatment develops an eruption, for it may be due to either drug or to the combination. Eruptions may result either from external application or internal administration. They may be due to an idiosyncrasy on the part of the patient or may occur as a part of a general mercurial intoxication resulting from too prolonged use or overdosage of mercury. Cessation of the drug usually results in disappearance of cutaneous manifestations.

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TREATMENT OF IVY POISONING BY RHUS TINCTURE AND ANTIGEN

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Until Strickler[1] developed his method of the treatment of ivy poisoning by the internal administration of tincture of rhus and the intramuscular injection of an antigen prepared from the plant, the treatment of a well established case was purely expectant. All kinds of lotions and salves were recommended, and many drugs were employed for internal administration, but there is no evidence that anything did any good except what a wise physician has called "tincture of time." These remarks do not apply to the mild and especially to the early cases, when there is no more than a little itching and a few small vesicles: in most of these cases thorough and repeated washing with soap and warm running water is effective, as we know from personal experience as well as by trial on others; and there is good evidence that applications of a warm slightly acidulated 1 per cent. or 2 per cent. solution of potassium permanganate is also effective. The soap and water treatment is useless, however, after the dermatitis has gone on to a diffuse swelling and the development of a mass of vesicles. The symptoms at this stage are sometimes severe, including fever, prostration, and discomfort sufficient to force the patient to forego all his ordinary occupations, and until Strickler's method was made available no real relief could be promised. This method has been on trial for a year or more, but as yet there have been few reports of its value. The cases here recorded are, with the exception of two private patients of one of us, from the various services of the New York Skin and Cancer Hospital. The table gives a summary of the results obtained.

Of the twenty-six cases enumerated in the table, fifteen showed definite improvement after the first dose; in five, the inflammation seemed to be checked by the first dose, and definite recession of symptoms occurred after the second; in five cases, improvement began after the second dose; while in only one was no improvement observed until after the third dose.

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1. Strickler, Albert: The Value of the Toxin (Antigen) of Rhus Toxicodendron and Rhus Venenata in the Treatment and Desensitization of Patients with Dermatitis Venenata, J. A. M. A. **80**:1588-1590 (June 2) 1923.

The most striking feature to the observer was the rapid improvement, usually after a single dose, which was observed in early and in late, in mild and especially in severe cases, some of which had been treated without success by other methods. Such rapid improvement, in all stages and grades of the eruption, can hardly be ascribed to chance.

Most of the patients received soothing local applications in addition to constitutional treatment, but some of them did not, and we are convinced that local applications have only a secondary value, if indeed they have any value. Some of them received the tincture of *Rhus toxicodendron* by mouth, and this probably did some good, as instances of its prophylactic and curative value when used alone have been observed.

Author's Results with Treatment of Ivy Poisoning by Rhus Tincture and Antigen

Duration from First Symptom to First Treatment Days	Condition	Number of Injections	Improvement Observed After Injection Number
2	Moderate	1	1
2	Severe	3	1–2
3	Very severe	4	3
4	Severe	2	2
4	Mild	2	1
4	Mild	2	2
5	Moderate	2	1
5	Moderate	3	1–2
6	Severe	3	1–2
7	Moderate	2	1
8	Mild	2	2
8	Severe	2	1
8	Severe	2	1
8	Severe	2	1
8	Severe	2	1
9	Severe	2	1
9	Moderate	2	1
9	Severe	4	1
14	Very severe	3	1–2
16	Mild	2	1
16	Mild	2	2
20	Severe	4	1–2
24	Moderate	2	1
35	Severe	2	1
..	Moderate	1	1
..	Severe	3	2

The antigen used in all cases was that prepared from *Rhus toxicodendron*, as *Rhus venenata* is uncommon in the vicinity of New York City, and is usually found in swamps, so that there is little chance of touching it. The dose given varied from 0.25 to 1.5 c.c. at each injection, at intervals varying from twenty-four to seventy-two hours. The pain of the injection is not great and seldom lasts more than a few hours. The smaller doses were used in the earlier cases of the series, but experience showed that the larger doses were equally well

borne and were much more effective. We believe that the initial dose of the antigen should be 1 c.c. We have observed no ill effects, and we believe that this method is the only satisfactory means at our disposal for treating one of the most annoying and often disabling incidents of summer time.

Abstracts from Current Literature

MALIGNANT GROWTHS IN NATIVES OF SIERRA LEONE. S. ADLER and E. H. T. CUMMINGS, Ann. Trop. Med. & Parasitol. **17**:535 (Dec. 21) 1923.

The authors state that sarcoma and carcinoma are rare among the natives of West Africa. However, in recent years these cases appear to be increasing. Whether this is due to European mannerisms or to increasing intelligence of the natives which causes them to seek medical advice more frequently, is hard to say.

In seven patients examined they found melanotic sarcoma in one, epithelioma of the scrotum and the lip, meningosarcoma, two cases of primary carcinoma of the liver and one case of secondary carcinoma of the liver.

THE ACUTE EXANTHEM OF LEPROSY. F. DE P. BARRERA and A. PENA CHAVARRIA, Bull. Johns Hopkins Hospital **35**:47 (May) 1924.

The cutaneous manifestations of the acute exanthem of leprosy consist of erythema and nodules which are at their beginning perceptible only by the sense of touch; later they become elevated above the skin. The patients complain of a burning pain in these nodules. The nodules vary in size from that of a millet to 3 cm. The skin may be incised and the nodules squeezed out, although the base is somewhat adherent. Occasionally nodules unite and form a leproma. These nodules may undergo involution or may ulcerate. The discharge contains the lepra bacilli. The acute exanthem may be the first manifestation of leprosy which until its occurrence has remained latent and unrecognized. During this exanthem, there is a characteristic temperature; when the temperature subsides, the eruption, nodules and ulcers disappear. The acute exanthem may determine the change of chronic tubercular leprosy into the maculo-anesthetic form or vice versa. The chronic nephritis and pulmonary tuberculosis of leprosy are the usual causes of death. It is a toxic manifestation. The urine in acute leprosy contains the lepra bacilli. The authors found the lepra bacilli in the blood in one case, and believe that during febrile exacerbations Hansen's bacilli may frequently be found in the blood.

The so-called lepra cells common in the chronic tubercle are not seen in the acute nodules. The lepra bacilli are few in acute nodules as compared with chronic leproma.

The acute nodule always occurs with fever, and is painful. The chronic tubercle occurs in conjunction with macules, alopecias and areas of anesthesia. Erythema nodosum is sometimes confused with the acute form of leprosy.

In conclusion, the authors state that leprosy has been regarded as a chronic condition. This is not the case, as the clinical course may frequently be interrupted by acute attacks, a fact which makes it necessary to regard leprosy in a new clinical light.

A CASE OF ARSENIC DERMATITIS IN A CHILD, TREATED WITH SODIUM THIOSULPHATE. CHARLES R. BUGG and CASPER FOCKOFF, Bull. Johns Hopkins Hospital **35**:76 (March) 1924.

The authors report the case of a child 2 years and six months old, who after six injections of sulpharsphenamin (0.22 gm.) at weekly intervals developed

a marked eczematous and exfoliative type of dermatitis, which responded well to intravenous injections of sodium thiosulphate. The drug was given in four graduated doses, a total of 1.35 gm. being sufficient to cause practically complete disappearance of the skin lesions in the course of six days.

Impetigo Contagiosa in Children—Its Etiology and Treatment. D. T. Smith and E. F. Busky, Bull. Johns Hopkins Hospital **35**:78 (March) 1924.

The authors report a series of nine cases of impetigo contagiosa, hemolytic streptococci being isolated in six and *Staphylococcus aureus* in three instances.

The streptococci are not of the same group either serologically or culturally. The staphylococci are not of the same serologic group.

Ammoniated mercury ointment (one-third the usual strength) is an effective treatment for the streptococcus but not for the staphylococcus cases.

Gentian violet (5 per cent.) is effective in the treatment of both staphylococcus and streptococcus impetigo.

A Typical Distribution of Varicella Lesions Dependent Upon a Coexistent Syphilitic Infection. W. S. Tillet and I. M. Rivers, Bull. Johns Hopkins Hospital **35**:137 (May) 1924.

The authors report a case of varicella in which the eruption was most marked over the face, scalp and extremities instead of over the trunk. The unusual distribution of the lesions in this case is believed to have been dependent on a coexistent syphilitic infection. The distribution of the lesions in this case corresponds closely to the usual distribution of lesions in congenital syphilis. The cutaneous distribution of many of the exanthems is directly influenced by irritation of the skin. The child in question had all the characteristic signs of congenital syphilis as well as a four plus Wassermann reaction.

A Case of Diabetes Refractory to Insulin Relieved by Antiluetic Treatment. Paul H. Charlton, Endocrinol. J. **8**:235 (March) 1924.

A patient with diabetis mellitus, polyuria, blood sugar 500 mg. per 100 cubic centimeters and urine sugar 2.2 per cent., also had pulmonary tuberculosis.

Insulin, beginning with three units three times a day and continued up to 34 units three times a day, was given for a period of four weeks. The blood sugar content remained the same. After discontinuing insulin for ten days, glycosuria increased to 4.8 per cent. The Wassermann reaction was found to be 2 plus. Antisyphilitic treatment was begun, and after three weeks the urine became sugar free, and the blood sugar fell to 140 mg. per 100 cubic centimeters. The patient died, and necropsy showed that the islands of Langerhans were found to be almost completely lacking.

McCafferty, New York.

Effects of the Long Continued Ingestion of Tyramine and Histamine. Robert McGarrison, Indian J. M. Res. **11,** No. 4, p. 1137.

Tyramin and histamin were fed to pigeons and white rats to ascertain the effects in the thyroid and suprarenals and certain facts relative to growth, respiration body temperature, etc. White rats which received tyramin and hystamin suffered from irritation of the skin, which, due to continual scratch-

ing first, became denuded in patches and later small pigmented scars. The hair was scanty and lacked luster. Growth was retarded. Respiration was depressed. The thymus and thyroid were reduced in size. Histamin caused an increase in size of the suprarenals in young rats. Tyramin caused a less marked but similar increase in both rats and pigeons. Contradictory effects were obtained with the two substances on some organs. Adult animals gradually overcame the effects of ingestion of the amins.

GUY, Pittsburgh.

ISOLATION OF THE DUCREY BACILLUS. J. BRAMS, J. A. M. A. **82**:1166 (April 12) 1924.

In a preliminary report, this investigator announces the isolation of Ducrey's organism from the smegma of five out of thirty healthy men examined. This study explains many heretofore unknown phases of chancroidal infection. These may be thus enumerated:

Persons apparently normal may be carriers of the Ducrey bacillus. A person need not necessarily acquire chancroid during sexual intercourse with an infected partner. The so-called mixed infection does not mean that the person was exposed to a partner who had both chancroid and chancre.

CONVALESCENT WHOLE BLOOD, PLASMA AND SERUM IN PROPHYLAXIS OF MEASLES. A. ZINGHER, J. A. M. A. **82**:1180 (April 12) 1924.

In an extensive study of this question, Zingher found that convalescent measles serum, plasma or whole blood confers complete passive immunity if injected within four to five days after exposure. In marasmic, rachitic, very young, or chronically ill, children complete immunity is desirable, since the mortality from measles in children with these diseases is high. A partial immunity leading to a modified mild form of measles may be achieved by these measures and can be used in healthy children, particularly those seen in private practice.

Of 102 nonimmune children receiving injections at varying intervals after exposure to measles, ninety-two were completely protected, seven developed modified measles, and two developed typical measles. Of the five control children, four developed typical measles.

A SURVEY OF ULCUS TROPICUM. T. CORPUS, J. A. M. A. **82**:1192 (April 12) 1924.

This condition is usually found in children, occurring most often on the legs. The ulcer is ordinarily rounded or oval and unilateral. It is contagious. Spirochetes (Eggert's Type A) were found in 35 per cent. of the cases, and are believed to be causative. A 3 per cent. arsphenamin solution applied locally gave the best therapeutic results.

THE DERMATOSES DUE TO COSMETICS. H. N. COLE, J. A. M. A. **82**:1909 (June 14) 1924.

In his chairman's address before the Section of Dermatology and Syphilology of the American Medical Association, Cole calls attention to the increasing use of cosmetics and the dangers inherent in these preparations. Practically all

these substances contain one or more of the heavy metals, as well as salicylic acid, wood alcohol, phenol and other chemicals with potentially dangerous properties.

Of the dyestuffs employed for rouging or for tinting the hair, the most harmful of all is paraphenylendiamin. It is in common use, and may give rise to a particularly severe and refractory dermatitis.

Cole thinks that the medical profession should take active steps to miminize the dangers of these preparations and suggests education of the public through the personal efforts of physicians, through publicity, and by governmental regulatory measures.

BILIRUBIN DETERMINATIONS IN THE BLOOD AS A MEASURE OF LIVER DAMAGE IN TREATMENT WITH THE ARSPHENAMINS. J. F. SCHAMBERG and H. BROWN, J. A. M. A. **82**:1911 (June 14) 1924.

The authors state that it is of value to have an index of liver toleration during arsphenamin treatment, since jaundice due to vulnerability of the liver is a not uncommon complication of arsphenamin treatment. Using van den Bergh's test, the authors examined a number of patients for hyperbilirubinemia. They were able to forecast the onset of jaundice by the test, and to determine the behavior of the liver under arsphenamin therapy. Thus, by this procedure, liver damage may be averted in some cases. It may also serve to determine when a damaged liver will permit the resumption of treatment.

The authors suggest that bilirubin determinations be made from time to time in patients receiving arsenical therapy as a guide to the toleration of the drug by the liver.

LEPROSY: REPORT OF SPORADIC CASE DEVELOPING IN PENNSYLVANIA. H. H. HOLDERMAN, J. A. M. A. **82**:1927 (June 27) 1924.

The patient had a characteristic case of the disease. Previous to its onset she had resided in Portugal, Brazil and Panama.

VISUAL DISTURBANCE PRODUCED BY TRYPARSAMIDE. A. C. WOODS and J. E. MOORE, J. A. M. A. **82**:2105 (June 28) 1924.

This study from the Johns Hopkins Hospital, embraces 241 cases in which more than 3,000 injections of tryparsamide have been given. Of this number of cases, 17.8 per cent. presented untoward ocular symptoms. The authors divide the visual disturbances into subjective and objective reactions. The former occurred in twenty-four cases (10.2 per cent.); the latter in thirteen cases, 5.5 per cent. In five cases, the influence of tryparsamide was questionable.

The subjective manifestations complained of are "dazzling" sensations. There is no accompanying disturbances of vision, nor can anything abnormal be found on ophthalmologic examination. The objective manifestations comprise the foregoing subjective symptoms and in addition dimness of vision and concentric contracture of the form fields. These disturbances may progress, but have always fallen far short of blindness.

Subjective manifestations without objective signs of optic injury do not prevent further use of tryparsamide; the occurrence of objective reactions is, however, an absolute contraindication for further employment of the drug.

Preexisting syphilitic disease of the optic nerve or retina is not necessarily a contraindication to the use of tryparsamide. Before treatment is begun with the drug, every patient should have an ophthalmologic examination.

URTICARIA CAUSED SPECIFICALLY BY THE ACTION OF PHYSICAL AGENTS (LIGHT, COLD, HEAT, FREEZING, BURNS, MECHANICAL IRRITATION, AND PHYSICAL AND MENTAL EXERTION. W. W. DUKE, J. A. M. A. **83**:3 (July 5) 1924.

Duke reports a number of cases of urticaria produced by physical agents. The reactions may be either contact (limited to the area to which the physical agent is applied) or diffuse (spreading out from the point of contact). In these cases there was no apparent allergy to protein substances. In most of the patients a constitutional response was demonstrable, such as eosinophilia.

In those cases apparently due solely to mental stress, the production of heat is probably either a contributing or essential factor.

A number of interesting hypotheses relating to immunologic responses are raised by these observations.

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USE OF SULPHARSPHENAMIN IN VINCENT'S ANGINA AND STOMATITIS IN CHILDREN. L. H. BARENBERG and M. W. BLOOMBERG, J. A. M. A. **83**:25 (July 5) 1924.

The authors have treated fifteen patients who had Vincent's angina and twenty-seven who had stomatitis, with intramuscular injections of sulpharsphenamin, combined in some cases with local applications of the drug. Prompt cure resulted, no patient requiring a second injection. Sulpharsphenamin is particularly desirable in the treatment of children with this disease because of the ease of administration.

THIOSINAMIN IN THE TREATMENT OF ARSPHENAMIN DERMATITIS. S. S. GREENBAUM, J. A. M. A. **83**:38 (July 5) 1924.

Thiosinamin is preferred by the author to sodium thiosulphate for the treatment of arsphenamin dermatitis. It is given intravenously in 3 grain (0.19 gm.) doses. A number of illustrative cases are recorded.

THE PREVENTION OF SCARLET FEVER. G. F. DICK and G. H. DICK, J. A. M. A. **83**:85 (July 12) 1924.

After briefly reviewing their investigation of the causation of scarlet fever and bringing forward additional proof that the streptococcus isolated by them is the causative organism, the authors report their observations on the prevention of the disease.

Immune persons give a negative skin test to scarlet fever toxin and require no precautionary measures. Nonimmune persons may be immunized by three doses of toxin, the development of a negative skin test constituting, however, the criterion of immunity.

In nonimmune persons who have been exposed to scarlet fever, the choice of procedure depends on the presence or absence of hemolytic streptococci in the throat. If throat cultures are negative, active immunization with scarlet fever toxin is carried out. If positive cultures are obtained, passive immunization with convalescent scarlet fever serum is accomplished.

The authors carried out these measures on 125 exposed persons, none of whom contracted the disease. Controls were afforded by physicians and nurses in the same hospital. Seven cases of scarlet fever developed in thirty-two controls.

Severe Reactions in Intraspinal Injection of Auto-Arsphenamized Serum. C. A. Kiely, J. A. M. A. **83**:108 (July 12) 1924.

The author reports one fatality and two serious reactions following intraspinal injections of auto-arsphenaminized serum prepared according to Kolmer's technic. The untoward results were traced to the employment of impure sodium citrate in preparing the serum.

Syphilis as a Complication of Pregnancy in the Negro: Analysis of Three Hundred Cases; Results of Antisyphilitic Treatment; Dark Field Examination as Aid in Diagnosis of Fetal Syphilis at Necropsy. R. A. Bartholomew, J. A. M. A. **83**:172 (July 19) 1924.

The author compared the pregnancies of 100 nonsyphilitic, untreated syphilitic and treated syphilitic patients. The syphilitic patients had three times as many abortions and seventeen times as many stillbirths as the nonsyphilitic patients. Antisyphilitic treatment during pregnancy led to a decided reduction in the abortions and stillbirths.

A dark-field examination of a suspension of liver substance obtained at necropsy or by aspiration is recommended as a valuable aid in diagnosing syphilis in babies stillborn or dying shortly after birth.

Nonsyphilitic Psychoses in Syphilitic Patients. William House, J. A. M. A. **83**:239 (July 26) 1924.

When syphilis is found in a psychotic patient it is often mistakenly considered causative. It should be remembered that a psychotic patient may acquire syphilis. While the patient should be treated for syphilis, if treatment is wholly directed to this condition less benefit will accrue than if a proper evaluation of its relation to the psychosis is understood. Every patient with a psychosis and syphilis should receive careful psychiatric examination.

Serologic and Clinical Results in Various Types of Syphilis with Sulpharsphenamin Administered Intramuscularly. J. H. Stokes and C. W. Behn, J. A. M. A. **83**:242 (July 26) 1924.

The authors' experience comprises 126 patients of all types, to whom 1,360 injections were given. They used a 30 to 40 per cent. solution, giving from 0.3 to 0.6 gm. at a dose.

The local reaction and discomfort at the site of injection was negligible. The drug has a vigorous spirillicidal effect; spirochetes disappeared from the chancres within ten hours. Early secondary lesions healed on the average in six days, chancres within seven to ten days. The results on the Wassermann reaction in early cases equals that previously obtained with arsphenamin and is superior to that of neo-arsphenamin. No neurorecurrences have developed. In latent syphilis, the effect on the Wassermann reaction has been good; of twenty-one patients who received sulpharsphenamin and mercury, fourteen became serologically negative, four were reduced from strongly to weakly positive, two were unchanged, and one failed to have a Wassermann reaction repeated. Some of these patients had received previous treatment without any effect on the blood reaction.

The effect on neurologic syphilis was superior to that obtained previously with arsphenamin. Late syphilids respond well from the clinical standpoint.

One course of sulpharsphenamin reversed the Wassermann reaction in 30 per cent. of these cases.

The drug is well borne by patients with cardiovascular syphilis if used in moderate doses. Eleven Wassermann-fast patients became serologically negative after one course of sulpharsphenamin and mercury.

Cutaneous reactions appear more frequently with sulpharsphenamin than with other arsenicals.

As the authors have been using the drug only fourteen months, it is impossible to say that the effects are lasting.

MICHAEL, Houston, Texas.

STUDIES ON VARICELLA. THE SUSCEPTIBILITY OF RABBITS TO THE VIRUS OF VARICELLA. T. M. RIVERS and W. S. TILLETT, J. Exper. Med. **38**:673 (Dec.) 1923.

Rivers and Tillett believe that they have recovered a virus from cases of varicella, and that the results obtained from inoculating rabbits were not merely the result of nonspecific irritation. They also conclude that the localization of the virus in the human skin is influenced by irritation. It was found that testicular emulsions were capable of producing lesions in the cornea, skin and testicles of rabbits.

INCLUSION BODIES IN EXPERIMENTAL HERPETIC INFECTIONS IN RABBITS. E. V. COWDRY and F. M. NICHOLSON, J. Exper. Med. **38**:695 (Dec.) 1923.

No inclusion bodies were found in herpetic lesions which could properly be interpreted as micro-organisms. The nature of the granules previously reported is still undetermined, though they believe that these granules do not represent a concrete class, but vary in composition, and arise from several sources.

ROENTGEN-RAY INTOXICATION: I. Bacterial Invasion of the Blood Stream as Influenced by X-Ray Destruction of the Mucosal Epithelium of the Small Intestine. S. L. WARREN and G. H. WHIPPLE, J. Exper. Med. **38**:713 (Dec.) 1923. II. The Cumulative Effect or Summation of X-Ray Exposures Given at Varying Intervals, Ibid., p. 725. III. The Path of a Beam of Hard Rays in the Living Organism, Ibid., p. 731. IV. Intestinal Lesions and Acute Intoxication Produced by Radiation in a Variety of Animals, Ibid., p. 741.

The intestinal epithelium is not considered the essential barrier which prevents invasion of the tissues by intestinal bacteria, as suitable doses of the roentgen ray will destroy the intestinal epithelium to a certain extent. This destruction, however, is not followed by an invasion of the tissues, blood and lymph by intestinal bacteria.

A sublethal roentgen-ray dose given over the abdomen will cause a definite injury to the small intestine mucosa, producing a clinical intoxication lasting from four to six days, the severity of the intoxication parallelling the epithelial injury. If small, repeated doses are given within a five or six day period, the sum of the doses equaling the single dose, the same result will occur, but roentgen-ray doses at intervals longer than six days show no evidence of summation.

The roentgen ray causing intestinal epithelial injury travels in straight lines from the target through the living tissues, controlled by screens to form a cone or a beam. Secondary radiation, if any, apparently does no harm except

to the intestinal epithelium in the path of the rays. It is possible to predict lesions of the stomach or intestine if it is known just how much roentgen ray and what form (cone or beam) is used over the abdomen; these lesions, however, do not heal, and may even cause perforation after many weeks.

Most of the common laboratory animals were found to be about equally sensitive to roentgen-ray doses over the abdomen, the rat and guinea-pig, however, being slightly more sensitive than the dog, cat and rabbit. Birds, frogs and reptiles are very resistant to the roentgen-ray, and may tolerate two or three times the lethal dose for dogs.

The writers believe that the human intestine is likewise sensitive to radiation, and warn against indiscriminate use in abdominal and pelvic conditons.

JAMIESON, Detroit.

RESULTS OF TREATMENT IN SYPHILIS OF THE NERVOUS SYSTEM. JOHN A. FORDYCE, Proc. Roy. Soc. Med. **17**:34 (March) 1924.

1. Invasion of the central nervous system occurs in the majority of cases during the period of general dissemination of the virus.

2. It is often checked but seldom cured by the usual therapeutic methods.

3. Late cases of neurosyphilis, including paresis and tabes, are not reinfections from foci outside the nervous system, but are due to long persistence of the infecting organisms in loco.

4. If the nervous system is not involved in the early period of the infection, it is extremely improbable that it will be in a later period. Vascular lesions and gummas may be expected.

5. In seeking for an explanation of the persistent positive Wassermann reaction in the so-called latent period, the possibility of a nervous system lesion should be kept in mind.

6. No patient should be discharged from treatment without the information afforded from a lumbar puncture.

7. Certain types of syphilis of the nervous system—including early meningitis, late meningovasculitis, tabes with positive phases in the fluid and with not too advanced degeneration in the lower cord, early optic atrophy with the findings of a meningitis—are more rapidly controlled by combined intravenous and intraspinal treatment and not infrequently only by this method.

8. In general paralysis, remissions of long duration are achieved which are more striking in patients with a pronounced meningeal reaction. Cures cannot be attained by any existing treatment.

9. As a result of the arsenic investigations pursued for the past two years, the authors have beeen able to detect arsenic in the spinal fluid of every person receiving intravenous treatment. An explanation of the cures after intraspinal injections is not therefore wholly due to the arsenic content of the serum, but possibly to the development of the antibodies in vivo.

Final judgment of a therapeutic procedure should be based on results rather than on theoretical reasoning.

GUY, Pittsburgh.

CONTRIBUTION TO OUR KNOWLEDGE OF FOX-FORDYCE'S DISEASE. OSKAR KIESS, Dermat. Wchnschr. **78**:1 (Jan. 5) 1924.

The author describes a typical involvement of the axillary and pubic regions, of two years' duration, in a woman, aged 33, this being probably the first clear-cut case of this affection to be reported in Germany. Photographs, photomicro-

graphs and a histologic report are included, and the author shows clinical and histologic proof that the disorder is not identical with neurodermite. He found no effective treatment.

DARIER'S DISEASE IN TWO GENERATIONS. W. H. SCHNEIDER, Dermat. Wchnschr. **78**:9 (Jan. 5) 1924.

The father, aged 42, presented an eruption of wide distribution, which had first appeared thirty years previously as "warts" on the hands. The oldest child, a boy aged 11, showed a miniature eruption with the same distribution as the father's. Histologically, the condition was Darier's disease. Both father and son were mentally subnormal.

THE PATHOGENESIS OF ARSPHENAMIN DERMATITIS. ERWIN PICK, Dermat. Wchnschr. **78**:15 (Jan. 5) 1924.

A syphilitic patient who had received courses of neo-arsphenamin and mercury became sensitized to both. The skin was apparently the only organ which reacted in this case, and a local reaction followed the local application of the arsphenamins. Other substances and other compounds of arsenic failed to produce the reaction, which was therefore attributed to the arsphenamin molecule rather than to the arsenic.

THE COLLOIDAL REACTIONS OF THE CEREBROSPINAL FLUID IN PRACTICE. V. KAFKA, Dermat. Wchnschr. **78**:23 (Jan. 5) 1924.

The author recommends the examination of the fluid as a check on the effectiveness of treatment, and at the same time stresses the importance of clinical observation.

THE REFRACTORY CHARACTER AND PECULIARITIES OF THE CLINICAL COURSE AND SEROLOGIC REACTION DURING THE TREATMENT OF SYPHILIS WITH SULPHOXYLATE ARSPHENAMIN. E. NATHAN, Dermat. Wchnschr. **78**:42 (Jan. 12) 1924.

In four cases of primary syphilis under this treatment, *Spirochaeta pallida* persisted in the sores, and the secondary rash appeared, but a negative serologic reaction was secured, indicating, according to the author, that this drug, of low spirocheticidal value, may exert some biologic effect on the tissues, which keeps the serum negative.

THE TREATMENT OF SYPHILIS WITH BISMUTH EXCLUSIVELY. ANDREAS GAAL, Dermat. Wchnschr. **78**:50 (Jan. 12) 1924.

In four cases of syphilis of one to three years' duration, a recurrence of lesions and serologic positivity followed this treatment.

INTRAVENOUS BISMUTH THERAPY. C. GUTMANN, Dermat. Wchnschr. **78**:73 (Jan. 19) 1924.

The intravenous injection of this bismuth preparation or its sodium salt in aqueous solution is recommended for general use, combined with occasional courses of the arsphenamins. Later in the course of treatment the bismuth may also be given intramuscularly.

SEVERE STRICTURE AS THE RESULT OF RECURRENT URETHRAL HERPES. E. KLAUSNER, Dermat. Wchnschr. **78**:82 (Jan. 19) 1924.

In this case, intra-urethral chancre was simulated.

A CASE OF MULTIPLE TUBEROUS HEMANGIOMAS. OTTO MARX, Dermat. Wchnschr. **78**:97 (Jan. 26) 1924.

In a child, aged 2, the tumors were of one month's duration, small but numerous, and of general distribution. Individual tumors resembled those of hemangio-endothelioma tuberosum multiplex, but the localization differed, as well as the histologic picture. A histologic drawing is shown.

DIFFERENCE IN VIRULENCE AMONG FAMILIES OF THE TRICHOPHYTONS. ERNST ROSENBAUM, Dermat. Wchnschr. **78**:99 (Jan. 26) 1924.

The author cites a case to show the occurrence of both slight and severe lesions due to the same organism in the same person, and he also describes various manifestations of infection with the same parasite in a mother and her two children, one of whom presented a typical picture of eczema marginatum.

THE FINDING OF SPIROCHAETA PALLIDA IN CONGENITAL SYPHILIS OF THE NEW-BORN, AND OBSERVATIONS ON A PATIENT TREATED WITH BISMUTH. C. BRACKMEYER, Dermat. Wchnschr. **78**:100 (Jan. 26) 1924.

In five of seven cases, the organisms were found in serum taken from papules and rhagades, and in that obtained by irritation from the nasal mucosa. There was no patient with coryza in the series of ten. No spirochetes were found in the urinary sediment. In two of the ten cases, the organisms were found in the venous blood. A case is cited to show the value of bismuth preparations in the treatment of congenital syphilis.

NEUROTROPIC SPIROCHETES AND DISPOSITION. G. NORDMANN, Dermat. Wchnschr. **78**:65 and 104 (Jan. 19 and 26) 1924.

After an extensive review of the literature on both sides of the question, the author cites cases and concludes that although there may be a neurotropic strain of the organism, the influence of treatment and terrain (individual disposition) are apparently of the greatest importance in determining the localization of late involvement.

A CASE OF POSTEXANTHEMATOUS TUBERCULOSIS OF THE SKIN. ERNST WIRTH, Dermat. Wchnschr. **78**:125 (Feb. 2) 1924.

In a child, aged 12, an attack of measles had been followed by phlyctenular conjunctivitis of three months' duration; then there had appeared lesions of tuberculosis verrucosa cutis and papulonecrotic tuberculids, in which the presence of tubercle bacilli was demonstrated histologically and by animal inoculation. The literature is reviewed.

QUININ IDIOSYNCRASY. ERWIN PICK, Dermat. Wchnschr. **78**:157 (Feb. 9) 1924.

In a girl who had been using a quinin ointment for five weeks, an eczematoid and urticarial eruption appeared, especially at the site of application, where

tests showed the idiosyncrasy to be most pronounced. The internal administration of quinin was followed by the reappearance of the eruption in the original areas.

A New Species of Scopulariopsis (Bainier): Scopulariopsis Castellanii. Masao Ota and Ginji Komaya, Dermat. Wchnschr. **78**:163 (Feb. 9) 1924.

The organism and its cultural characteristics are described, and animal experiments are recounted.

The Combined Use of Tincture of Iodin and White Precipitate Ointment in Dermatoses. Otto Sachs, Dermat. Wchnschr. **78**:165 (Feb. 9) 1924.

Already found serviceable in the treatment of lupus erythematosus, the application of the tincture, soon followed by the ointment in 5 per cent. strength, is recommended by the author for use in superficial ringworm infections.

The Serologic Diagnosis of Syphilis According to Bruck. H. Muchow, Dermat. Wchnschr. **78**:166 (Feb. 9) 1924.

The author finds the Bruck method to be highly specific, and valuable when used in conjunction with other serologic tests.

Attempts at Provocation in the Wassermann-Negative Stage of Syphilis. Ernst Radnai, Dermat. Wchnschr. **78**:168 (Feb. 9) 1924.

In two cases in which injections of the arsphenamin brought no positive Wassermann reaction, the use of a nonspecific milk preparation or bismuth intramuscularly was followed by serologic positivity.

Lupus Erythematosus and Carcinoma. Seigo Minami, Dermat. Wchnschr. **78**:213 (Feb. 23) 1924.

Less frequently than in lupus vulgaris, prickle cell epithelioma may accompany lupus erythematosus. The author reports a case occurring in a man, aged 28, with lupus erythematosus of eleven years' duration, who had been treated by roentgen-ray exposures during the second year. The literature is reviewed, fourteen authors being quoted.

The Action of Bismuth Preparations on the Syphilitic Organism. Eduard Neuber, Dermat. Wchnschr. **78**:185 and 237 (Feb. 16 and 23) 1924.

Bismuth was found unsuitable for the abortive treatment of early syphilis, and its effect on the Wassermann reaction was weaker than that of either mercury or arsphenamin. It was better borne than mercury, and useful in combination with arsphenamin. In two cases of gumma, bone and the tongue being affected, which proved refractory to arsenical and mercurial medication, the use of bismuth was successful.

The Morphology, Biology and Classification of the Pathogenic, Asporogenic Budding Fungus (Sproszpilze). Masao Ota, Dermat. Wchnschr. **78**:216 and 260 (Feb. 23 and March 1) 1924.

All the organisms without mycelia or their anlagen are classified as cryptococci, while those possessing mycelia or their anlagen are called mycelo-

blastanons, under which classification appear *Blastodendrion, Mycelorrhizodes* and *Monilia.* To the family of *Parendomyces* belong those organisms which besides producing the garland-shaped "arthrospores," also produce true "blastospores" at some stage of their life cycle. The *Mycoderm* family can also produce spores, especially at an early stage.

THE CALCIUM CONTENT OF NORMAL AND PATHOLOGIC SKIN. OSKAR GANS and THEODOR PARKHEISER, Dermat. Wchnschr. **78**:249 (March 1) 1924.

The authors report the results of microchemic studies in various eczemas as compared with the normal, and speculate as to the colloid changes which accompany alterations in the calcium content.

THE NATURE OF ECZEMA. CARL KREIBICH, Dermat. Wchnschr. **78**:277 (March 8) 1924.

The author concludes that eczema is a punctiform dermatitis factitia, brought on by mechanical, physical or chemical irritation, its course being either acute or persistent through itching.

NEW PATHOGENIC YEASTS OF THE DEBARYOMYCES FAMILY. MASAO OTA, Dermat. Wchnschr. **78**:284 and 312 (March 8 and 15) 1924.

Under this classification the author includes the yeast causing the erosio interdigitalis blastomycetica of Fabry and also *Saccharomyces emphysematosus,* which Grutz isolated from infected nails. The latter is pathogenic for the mouse. Neither produces mycelia.

A MICROSPORON ENDEMIC IN CHEMNITZ. RICHARD FRÜHWALD, Dermat. Wchnschr **78**:333 (March 22) 1924.

Seventeen cases occurred in a children's home, the causative organism being *Microsporon audouini.* The scalp was generally involved, but in three cases the organisms were recovered from patches on the glabrous skin. The histologic findings are recorded. Epilation by means of the roentgen rays was used with success.

THE EVALUATION OF STAINED PREPARATIONS. RAPHAEL E. LIESEGANG, Dermat. Wchnschr. **78**:340 (March 22) 1924.

Explanations of staining processes are valuable not only in connection with histologic technic, but also in studying the distribution of drugs in the tissues.

THE DEMONSTRATION OF SPIROCHAETA PALLIDA IN CIRCULATING BLOOD IN CONGENITAL SYPHILIS. A. BUSCHKE, Dermat. Wchnschr. **78**:344 (March 22) 1924.

Referring to the recently abstracted article of Brackmeister, which appeared in this publication, the author remarks that with W. Fischer in 1906 he found the organisms in the blood of a child with congenital syphilitic myocarditis.

Book Review

HANDBOOK OF SKIN DISEASES. By FREDERICK GARDINER, Physician of Diseases of the Skin, Royal Infirmary, Edinburgh. Pp. 246. Price, $3.00. New York: William Wood & Company, 1924.

We note with pleasure the appearance of the second edition of Gardiner's handbook. It is an excellent little book. It is difficult to write an introduction of this kind on skin diseases. Most books fail by simply being attempts at condensing the knowledge of the subject and stating it in as few words as possible. Gardiner does not do this. He draws an outline of dermatology as illustrated by the commoner diseases and with a background of knowledge of the whole subject in the author's mind. This is apparently a trait of the Edinburgh school. The reviewer remembers with what pleasure, as a young man, he read Allan Jamieson's "Diseases of the Skin," because it had this philosophical touch, and Gardiner's book in a way reminds one of Jamieson's. It is not an epitome of skin diseases, but it is an excellent introduction to the subject, and can be read with interest by any one interested in dermatology.

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